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UNUSUAL METASTATIC MANIFESTATIONS OF BREAST CARCINOMA

I. Metastasis to the Mandible with a Report of Five Cases

FRANK E. ADAIR, M.D., F.A.C.S., and JULIAN B. HERRMANN, M.D., New York, New York

PERTHES in 1907 wrote, "the rarest form of jaw carcinoma is the metastatic." Almost 40 years have elapsed since this observation was recorded, yet its validity has remained unchallenged. During this period roentgenology, the greatest aid in the diagnosis of osseous metastases, had its origin and development. Evidently the paucity of reported instances of metastatic involvement of the mandible cannot be ascribed to the inadequacy of diagnostic facilities during these years. As recently as 1936, Geschickter stated that "although carcinoma metastasizing to bone is a relatively common condition, the upper and lower jaw are rarely involved." It is conceivable that a metastatic focus in the mandible might remain asymptomatic and thus be overlooked, but such instances must be extremely infrequent.

Three lesions which frequently produce osseous metastases are carcinoma of the thyroid, prostate, and breast. Metastasis to the mandible from these primary sites, however, appears to be uncommon in thyroid carcinoma and extremely infrequent in breast and prostatic cancer. Rare examples of metastasis to the mandible from carcinoma of the lung, rectum and kidney have been reported (Stern and Shepard, Blum). Some authors (Ehrhardt, Blumer) have described a number of cases of metastasis of thyroid carcinoma to the mandible, but we have been able to find only 11 recorded instances of metastatic involvement of the mandible from carcinoma of the breast. To this number we add 5 of our own.

The earliest recorded case is that of Batzaroff who in 1829 described the occurrence of metastasis to the mandible 21 months after a mastectomy for mammary carcinoma. There was no evidence of local recurrence. There is no other reported example until 1909 when Schlesinger published reports of 5 cases of lower jaw metastatic lesions, 4 associated with carcinoma of the breast, and 1 with carcinoma of the prostate. About 20 years later, Blair, Brown, and Womack wrote that they had noted metastatic carcinoma of the jaw three times, once from the rectum and twice from the breast. No details were given.

In 1930 Sonntag described the case of a 65 year old woman who consulted him because of a swelling of the left lower jaw of several months' duration. She had undergone a left radical mastectomy 3 years previously. There was no evidence of metastasis elsewhere, therefore the mass in the mandible was considered a primary tumor and the jaw was resected. Microscopic examination revealed the jaw lesion to be metastatic mammary cancer. The patient died one year later. Skillen also in 1930 reported the case of a 40 year old

From the Breast Service of the Memorial Hospital, New York.

woman with a metastatic lesion to the mandible, proved histologically, from a breast carcinoma.

The same year (1930) Thoma, in his textbook gave an abstract of 2 cases. One, a 46 year old woman, developed a metastatic lesion in the left mandible following a mastectomy for colloid carcinoma of the left breast. The second patient developed a metastasis to the left mandible from an adenosarcoma of the left breast. It is of interest that Rogers and Flo have reported a case of metastasis to the mandible consequent upon a breast fibrosarcoma.

The most recent example published is by Burket in 1941. This was a 38 year old woman who developed metastatic disease in the right mandible 4 years after a left radical mastectomy for carcinoma.

Our 5 cases are as follows.

CASE 1. B.E., a 41 year old female, underwent preoperative irradiation and a right radical mastectomy 3 years before coming to the clinic. The pathological diagnosis was adenocarcinoma grade 3 with node metastasis. One year following the mastectomy the patient had an extraction of a left lower molar with subsequent numbness of the lower left side of the face and swelling of the left mandible. These symptoms persisted. Her chief complaints on admission were cough, dyspnea, pain in the chest and back, anorexia and occasional vomiting, and swelling of the left mandible.

Examination revealed a well healed right radical mastectomy scar. There was no evidence of local recurrence and no adenopathy. In the horizontal ramus of the left mandible near the junction of the middle and posterior thirds there was a smooth, hard, fixed, painless, nonulcerated mass about 2 centimeters in diameter, involving the whole thickness of the bone.

Roentgen studies disclosed evidence of metastasis to the pelvis and extensive destruction of the horizontal ramus of the left mandible (Fig. 1). An aspiration biopsy of the mass on the mandible was reported as metastatic carcinoma consistent with mammary origin. The patient was given a small amount of roentgen therapy to mandible but died of metastases about 4 months after her initial visit.

CASE 2. J.C., a 63 year old woman, consulted the clinic because of a lump of 18 months' duration in the right breast. The lump had been growing slowly until 2 months previously when it began to ulcerate. Examination revealed the right nipple and areola to be completely replaced by a hornifying crust and the central portion of the breast to be entirely filled by a stony hard tumor mass 6 centimeters in diameter. There was no palpable adenopathy.

The patient refused operative therapy and failed to return to the clinic for 2 years. Despite the elapsed time the condition was still operable although nodes were now palpable in the right axilla. A radical mastectomy was performed following which she made a good recovery. An area on the anterior right chest wall required a skin graft.

The pathological report on the surgical specimen was infiltrating duct carcinoma grade 3, with metastasis to the axillary lymph nodes. Because the grafted area was slow to heal the patient did not receive any postoperative x-ray therapy.

Her return visits to the clinic were irregular at first and then ceased for about 9 months. She then consulted the clinic because of the appearance of some nodules in the skin of the right chest wall at the edge of the previous graft. A biopsy of one of these nodules was reported as recurrent carcinoma and radiation therapy was advised. She failed to return for 8 months at which time low voltage irradiation was administered to the right anterior chest wall.

Another 4 months' period of absenteeism from the clinic followed. At the end of this interval the patient returned because of an enlargement in the right mandible and right temporal region. Examination revealed a hard swelling involving the right mandible. A roentgenogram disclosed numerous and extensive areas of bone destruction in the right mandible and skull which were interpreted as carcinoma metastases (Fig. 2). She received a small amount of x-ray therapy to the right side of the face but failed to return for further treatment and was lost to follow-up.

CASE 3. M.R., a 43 year old woman, underwent a radical mastectomy for carcinoma of the left breast in January, 1940. The pathological diagnosis was infiltrating duct carcinoma grade 3 with metastasis to multiple axillary nodes.

The patient remained free from apparent disease for about 2½ years. Then she developed a mass over the left third rib about 2 centimeters from the lateral border of the sternum. A roentgenogram disclosed an area of destruction in the anterior part of the third left rib. There was no other evidence of disease.

In view of the desperate situation the involved area of the rib was resected and at the same time the patient was sterilized, a panhysterectomy being performed. The pathological report on the excised tumor of the rib was "mammary carcinoma invading rib."

For about 1 year following this she was apparently free of disease. A roentgenogram of the chest at the end of this period failed to reveal any evidence of disease. A short time later, however, the patient developed paresthesia ("sensation of pins and needles") in the left side of her face. She considered the condition a neuralgia and treated herself. The paresthesia changed in character and became a sensation of numbness over the left lower jaw.

Several months later the patient developed pain in the lower dorsal region and a lump in the left lower

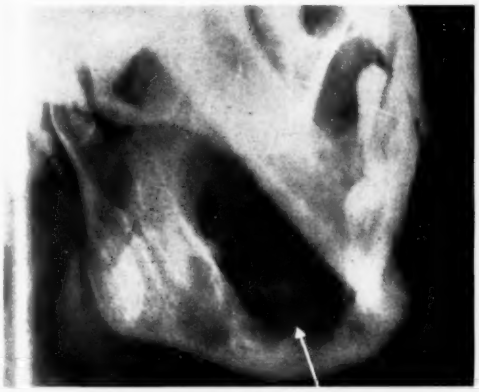

Fig. 1. Roentgenogram, Case 1, showing extensive destruction of the horizontal ramus of the left mandible.

Fig. 2. Case 2. Numerous and extensive areas of bone destruction in right mandible and skull are shown.

jaw. The sensation of numbness over the left mandible still persisted. An x-ray examination of the lumbar spine and pelvis revealed numerous areas of metastasis. Roentgenographic study of the mandible disclosed an area of destruction in the horizontal ramus (Fig. 3). There were also at this time metastatic deposits in the scalp and in the skin of the chest wall. She received x-ray therapy to all of the metastatic lesions and is still living with active disease 5 years after her radical mastectomy.

CASE 4. E.M. was a 51 year old woman who in 1936 underwent a simple mastectomy for carcinoma of the left breast at another institution. She was apparently free of disease for about 2 years. Then a swelling appeared over the angle of the right mandible for which she consulted this clinic. Roentgenographic studies revealed a large area of bone destruction in the ascending ramus of the right mandible (Fig. 4). The roentgenologist believed that it presented more of the features of a primary bone tumor such as an adamantinoma rather than those of metastatic carcinoma. The irregularities of bone destruction, and the somewhat honeycomb appearance, made a diagnosis of a primary bone tumor such as an adamantinoma seem more likely. Films of the chest failed to reveal evidence of a primary tumor or metastases. Roentgenograms of the pelvis, spine, legs and arms exhibited no evidence of bone destruction or carcinoma metastasis.

An aspiration biopsy of the mass in the mandible was performed and reported as adenocarcinoma consistent with mammary origin. A submitted slide of

Fig. 3. Case 3. An area of destruction in horizontal ramus is shown.

Fig. 4. Case 4. Roentgenogram reveals a large area of bone destruction in ascending ramus of the right mandible.

Fig. 5. Case 4. Four months later roentgenogram reveals considerable bone regeneration in the area of destruction about the angle of the mandible.

the original breast tumor was reported as infiltrating duct carcinoma grade 3, and this material was considered by Dr. Fred Stewart as perfectly consistent with that obtained from the mandible by aspiration.

The patient received x-ray therapy to the metastatic lesion in the mandible with considerable regression of the mass. A roentgenogram taken 4 months later revealed evidence of considerable bone regeneration in the area of destruction about the angle of the mandible (Fig. 5). Physical examination 2 years after this film was made revealed the right mandible to be slightly larger than the left near the angle.

Soon after this the patient developed anorexia, flatulence, and generalized abdominal pain. On examination a mass was found in the epigastrium. There was no other demonstrable evidence of disease. The patient's condition gradually deteriorated and she died in 1942, 6 years after the removal of the breast for carcinoma. An autopsy revealed metastatic adenocarcinoma in the liver, mediastinal, and peripancreatic lymph nodes. The metastatic cancer was reported as consistent with a mammary origin.

Case 5. M.P., a 50 year old woman, consulted the clinic in June, 1943, because of a lump in the left breast of 3 years' duration and because of irregular menstrual periods of 9 months' duration. Examination revealed the right breast to be elevated, the nipple retracted, and ulceration at the junction of the nipple with the areola. Beneath the areola was a hard, nodular 2 by 3 centimeter mass attached to the overlying skin. A hard mass was palpable in the right axilla. Pelvic examination disclosed a mass posterior to the cervix which was thought to be an ovarian tumor.

An aspiration biopsy of the breast mass revealed carcinoma; therefore a radical mastectomy was performed. The pathological diagnosis was infiltrating duct carcinoma grade 3 metastatic to the axillary lymph nodes at all levels. She received a cycle of postoperative x-ray therapy.

Upon the completion of the x-ray therapy a diagnostic curettage was done. The pathological report was adenoma malignum grade 2. The patient then received intrauterine radium therapy. Later a supracervical hysterectomy and bilateral oophorectomy were performed. The pathological report was corpus adenocarcinoma grade 2 and malignant endosalpingioma of the left ovary.

Following all of these procedures the patient remained in apparent good health for about 1 year. Then she began to have pain in the lumbar spine which upon roentgenographic studies was found to be in consequence of metastasis to the lumbar spine and pelvis. She received high voltage irradiation to these areas with amelioration of her pain.

About 5 months later she began to complain of pain in the knees. X-ray studies disclosed changes in the tibiae and lower left femur which were thought to resemble Paget's disease. For confirmatory evidence an x-ray plate of the skull was taken which revealed evidence of the presence of extensive diffuse destruction. This was interpreted as carcinoma metastasis. Blood chemical studies gave results which were consistent with bone metastasis but not with Paget's disease. The patient received x-ray therapy to the knees with subsidence of the pain.

Three months after this episode she began to experience pain in the right mandible. Examination of this area disclosed a small, swollen, tender area over the horizontal ramus. A roentgenogram of the right mandible revealed a large irregular area of bone destruction in the anterior half of the horizontal ramus (Fig. 6). The mandible was irradiated and the pain subsided.

Fig. 6. Case 5. Roentgenogram reveals a large irregular area of bone destruction in the anterior half of the horizontal ramus of the right mandible.

The lesion in the mandible could have been metastatic from any of the 3 primary lesions but on the basis of probability it most likely was secondary to that in the breast.

The first indication of metastatic disease of the mandible may be pain, frequently in association with a loose tooth. In these instances the patient is usually seen first by the dentist and the tooth extracted as in the case reported by Burket and in our own Case 1. It is only later that the underlying cause is recognized. Paresthesia on occasion may be an early sign of metastatic invasion of the mandible. This is exemplified by our Cases 1 and 3. Pressure on, or involvement of, the mandibular nerve by the disease produces pain or numbness which stops sharply at the midpoint of the symphysis menti.

In some instances paresthesia of the side of the face and of the buccal and gingival mucous membrane may persist for a long period of time without any evidence of involvement of the mandible. This phenomenon is illustrated by the following case.

E.F. was a 43 year old woman who underwent a right radical mastectomy followed by x-ray therapy for carcinoma 3 years before consulting this clinic. Examination revealed no evidence of disease. During the ensuing 18 months she developed metastatic nodules in the right chest wall and nodes in the left axilla. About the end of this period she began to experience a sensation of numbness in the skin of the lower right face over the mandible and in the corresponding buccal and gingival mucous membranes. This area of paresthesia was sharply delimited at its medial aspect by the symphysis menti. Roentgenographic studies of the skull, mandible, lumbar spine, pelvis, and chest failed to reveal any evidence of metastasis. Six months later the paresthesia was unchanged and repeat x-ray studies of the skull and mandible failed to reveal any changes. The patient lived 7 months longer and during this period the paresthesia persisted without any external evidence of mandibular involvement.

In some instances in which a single metastasis localizes in the mandible a number of years after a mastectomy for carcinoma, the true nature of the condition may be overlooked and a diagnosis made of primary mandibular neoplasm. This happened in Sonntag's patient, and the mandible was resected. In our Case 4 a primary malignant lesion of the mandible was suspected. There were no other foci of disease and the roentgenographic appearance was suggestive of a primary neoplasm. This would indicate that the roentgenogram may not always solve this type of diagnostic problem. In this connection New and Figi state that it is impossible to distinguish roentgenologically many of the primary tumors of the jaw from the metastatic malignant tumors. In some instances, however, aspiration biopsy may be of value, as in our Cases 1 and 4. By this procedure it may be possible to spare the patient a useless operation.

An interesting and perplexing problem is presented as a consequence of the finding that carcinoma of the breast manifests a predilection for certain osseous metastatic sites whereas other localities are relatively immune. Paget about 50 years ago commented on this saying "The evidence seems to me irresistible that in cancer of the breast the bones suffer in a special way which cannot be explained by the theory of embolism alone. Some bones suffer more than others; the disease has its seats of election." The theories of metastatic spread attempt to explain this phenomenon. A few of the more important theories will be briefly reviewed in an endeavor to elucidate an explanation for the infrequent involvement of the mandible.

Von Recklinghausen in 1891 was one of the first to suggest that malignant tumors metastasize to bone by means of the blood stream. According to this theory the tumor emboli become lodged in the marrow and develop a metastatic focus. His conclusion was based on the following observations: (1) Osseous metastatic lesions occur in the medullary cavity and reach the periosteum by direct extension. (2) If there is subperiosteal involvement it is always in the region of the large foramina which serve as an exit for the veins. (3) The cancer cells are found in definite channels within the marrow which he believed to be venous rather than lymphatic. It is suggestive that in 4 of the present series the lesion appeared in the horizontal ramus and in the fifth, the angle of the mandible was involved. This might be explained on the basis that hematogenous cancer emboli enter the medullary cavity through the mandibular foramen.

Handley advanced the theory that cancer is disseminated to bone by permeation through

the lymphatics. He believed that the bones nearest the breast, namely, the ribs and sternum were involved by direct extension but that the more distant ones were invaded by permeation of the cancer cells through the deep fascial lymphatics. Invasion of the bones took place at those points where they approached the skin and were consequently nearest the deep fascia. In the femur this was at the site of the great trochanter and in the humerus at the site of the deltoid insertion.

He explained the rarity of metastases to the forearm, hand, leg, and foot on the basis that lymphatic permeation was in general a slow process and that the patient died before it extended as far as the bones of the extremities. This explanation does not account for the infrequency of metastatic involvement of the mandible because the skull, which is further distant from the primary lesion than the mandible, is not infrequently the site of metastatic disease.

Carnett and Howell, while agreeing in essence with Handley's theory have advanced some important modifications. They believe that the humerus is invaded in most instances by direct permeation of the disease from the axillary lymph nodes which have become cancerous by lymphatic emboli rather than by permeation along the deep fascia of the chest wall. According to their conception the metastases localize initially in the head of the humerus and glenoid process of the scapula rather than at the deltoid insertion as suggested by Handley. The cervical vertebrae and skull are involved by a process of permeation and embolism extending from the axillary lymphatics along the infraclavicular and supraclavicular lymphatics beneath the deep fascia. The lumbar vertebrae and pelvis are involved by direct extension from the retroperitoneal lymph nodes which have become cancerous by permeation from the breast along the periaortic lymphatics. The invasion of the femur is by direct extension to the femoral head from the pelvis through the lymphatics of the ligamentum teres.

In recent years Batson has demonstrated that it is possible for material injected into the peripheral venous circulation to reach the spine, pelvis, and skull by way of the vertebral veins without passing through the lungs. This may be the pathway in some instances of metastatic spread.

It is well established that the skull is a common site of metastasis in breast carcinoma. Carnett and Howell in their series of 101 cases of osseous metastasis from breast carcinoma found the skull involved in 14 cases but mentioned no instance of mandibular involvement. Lenz and Fried in an analysis of 81 cases encountered skull involvement in 35 per cent and no instance of mandibular disease. If involvement of contiguous bones is by direct spread, as Carnett and Howell maintain, citing as an example invasion of the head of the femur from disease of the pelvis, then the mandible ought to be involved more frequently by direct extension from the skull. Furthermore if involvement of the mandible is by direct spread from the skull it would be logical to expect the region of the condyles to be invaded early. It appears, however, that when metastatic invasion of the mandible does occur it may be in the horizontal rather than in the ascending ramus. This was demonstrated by 4 of our cases.

An interesting theory has been suggested by Pinney. He believes that bone metastases are produced by blood borne emboli which lodge in the thin walled blood channels of the red marrow, and he has been able to demonstrate plugs of epithelial cells in this location. He was unable to demonstrate any lymphatics in bone marrow and concluded that they are absent. He postulates that not only must the cancer emboli reach the marrow but the current here must be slow enough to allow the cells to lodge and grow. These conditions are satisfied by the red marrow which, because of its great vascularity, produces a widening of the blood stream bed with a consequent slowing of the current.

The localization of bone metastases is explained by this theory on the basis of red bone marrow distribution. In the infant all the bones contain red marrow but by the time adult life has been reached this has been replaced by fat except in the skull, sternum, ribs, clavicles, scapulae, vertebrae, os innominatum, and the proximal portions of the ex-

tremities where red marrow continues to persist throughout life (Doan).

Pinney ascribes the infrequency of metastasis below the elbow and knee to the absence of red marrow in these locations. He believes that bone metastasis may occur occasionally by way of the lymphatics but that the principal route is hematogenous. It is probable that both lymphogenous and hematogenous routes are essential to bone metastasis.

Some investigative work carried out by Box is of interest in this connection. He examined numerous areas of a series of human jaws and in 75 per cent found only yellow marrow. In the remainder there were small, discrete areas of red marrow encountered. From his researches he concluded that even in early adult life the bone marrow in the average normal jaw is of the fatty or yellowish variety. In those instances in which small patches of red marrow were found he believed it was due to: (1) vestiges of original red marrow that had not undergone change; (2) local stimuli such as trauma from a tooth extraction, root canal filling, or gingival infection.

This infrequency of the presence of red marrow in the mandible might, on the basis of Pinney's theory, account for the rarity of metastasis to the mandible in breast carcinoma. The only contradictory evidence is furnished by Ehrhardt's report of 65 cases of malignant struma with bone metastases, 30 of which were to the mandible. This percentage is so high that it suggests the possibility that many of these were due to direct extension rather than metastasis.

SUMMARY

1. Eleven examples of metastasis to the mandible from breast carcinoma were found reported in the literature.

2. Five cases observed in this clinic are presented.

3. Various theories of metastatic spread are briefly reviewed in an attempt to explain the apparent immunity of the mandible to metastasis.

4. The explanation is advanced that the mandible is infrequently involved by metastatic disease because of the customary absence of red marrow.

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THE PELVIC FLOOR IN PARTURITION

RICHARD M. H. POWER, M.Sc., M.D., C.M., F.A.C.S., Montreal, Canada

THE orderly sequence of changes in the structure of the pelvic floor during parturition has received little or inadequate attention in recent publications. A consecutive account of what happens in the constituent structures of the floor during parturition seems opportune. While textbooks are spotty in their description of the structural anatomy, there is a manifest lack of consecutive description in the anatomical sequence of events, and particularly of the admirable structural adaptations for this natural event.

The enquiring senior students, after study and mature reflection, frequently ask: What happens to the much heralded fascial structures during delivery? How does the levator ani muscular diaphragm dilate? What becomes of the double leafed fascial structure, the urogenital diaphragm? How does it open up when the fetal head passes through it?

Briefly, at the moment of expulsion of the fetal head, the pelvic floor and the urogenital tract are converted into one continuous cleft (Figs. 1, 2, 14). At this moment, the lateral ligaments of the cervix uteri (Mackenrodt) are flattened in transverse, and elongated in vertical, section. The levator ani muscular diaphragm is funnelled. The urogenital diaphragm, or as it is more popularly known, "the triangular ligament," is opened up and closes again (Figs. 1 to 3, 5, 6, 10, 13 to 15). The smooth muscle diaphragm in the base of the broad ligament and the sphincteric group of muscles at the vulval outlet are dilated spherically. The latter are converted into a short muscular tube with the passage of the fetal ovoid.

Before these questions are answered in detail, and in order to avoid speculation, a brief anatomical preview of the pelvic floor is necessary.

From the Department of Anatomy, McGill University, and the Departments of Gynecology and Obstetrics, St. Mary's Hospital, Montreal. This work was partially assisted by a grant from the Cooper Fund of McGill University.

The pelvic floor is a musculofascial diaphragm. Extending into it posteriorly is a movable bony platform, the coccyx.

This musculofascial diaphragm is a composite structure of connective tissue, voluntary and smooth muscle and elastic tissue, arranged in five diaphragmatic layers, superimposed and interwoven one upon the other for reciprocal support. Neither singly nor united do these diaphragms form a complete sling or hammock across the pelvic floor, as they are perforated centrally by three tubular structures, the urethra, the vagina, and the anal canal. These canals are arranged very much like tubes passing through the shutters of a venetian blind. Their tubular openings are closed by the sphincteric arrangement of these musculofascial floors.

These diaphragms not only close the tubular openings, but serve as essential supports to the pelvic viscera; the endopelvic fascial and levator ani muscular diaphragms being the most essential. All five diaphragms have an anchorage into the perineal body. They are set at different planes (Fig. 3) and are fixed at different levels to the bony canal, which latter resembles the "elbow of a stovepipe." They act as so many floors of support to the viscera —placed like shingles—one gliding over the other in fluid movement, arranged that they may be dilated to their capacity as they are in parturition during the conversion of the pelvic floor into one large hiatus previous to expulsion. Dilatation of these floors occurs from above downward, and restoration comes about in the reverse order following delivery, provided their anatomical integrity has been maintained.

Trauma from childbirth is the principal cause of injury to the pelvic floor. Other causes may be congenital weakness, involution and atrophy of fat in old age, neurogenic injury to the fourth sacral nerve (spina bifida).

Following injury to any single or complete set of "uterine supports," prolapse may re-

sult. This prolapse may be complete or incomplete, as cystocele, where the anterior segment is injured, or rectocele with injury to the posterior segment, or sacropubic hernia, i.e., procidentia uteri, where anterior lateral and posterior segments are injured.

From above downward in anatomical order these diaphragms are as follows: (1) the endopelvic fascial diaphragm or upper pelvic fascial floor, (2) the smooth muscle diaphragm in the base of the broad ligament, (3) the levator ani muscular diaphragm, (4) the urogenital diaphragm, and (5) the sphincteric group at the vulval outlet.

While these composite structures differ in their development and in their function, nevertheless, collectively they are unique in their synchronous uniformity in response to functional demands. Their collective structural arrangement allows for marked excursions of distention and contractility.

Connective tissue is primarily a supportive structure in character. Fascia, in itself, is not unusually found in regions subjected to intermittent and varying degrees of tension. Usually it is most developed where it can respond as a passive elastic agent which must not be extended beyond its quantum of elasticity. Smooth or striated muscle, however, having the property of maintaining "tension" or "tonus" can withstand tension or stretching, which could not be tolerated by mere fascia. If, however, owing to nutritional or mechanical factors, its power of maintaining a high tonus is lessened, then it is a much less efficient supporting structure than is fascia. Smooth muscle has the property of maintaining, within fairly narrow limits, the same tonic force irrespective of the degree of stretch to which it is subjected until the limit of its elasticity is reached. From then on it behaves as an inactive fascial tissue. These considerations, when applied to the arrangements of the above tissues, are of fundamental importance. Smooth muscle tissue is found precisely in those regions where it is necessary to permit considerable dilatation, contraction, or movement of organs, meanwhile maintaining some degree of control of the movements of these organs independently and in relation to each other.

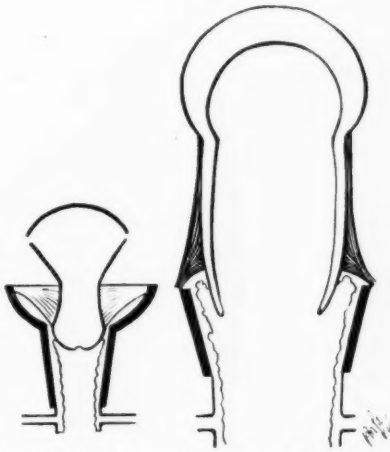

Fig. 1. Schematic representation. a, left, Structures at rest; b, uterovaginal canal converted into urogenital hiatus.

It is obvious that it is necessary to have a mechanism to restore the normal state after a major dilatation, etc., of one or more of the organs. It is equally obvious that fascia would be ineffective in such contingencies.

Dilatation of the connective tissue diaphragm, to the extent of permitting the passage of the fetal head, demands a great stretching of this poorly contractile tissue, which of itself could not assume its original dimensions as it contains little, if any, elastic tissue. Hence Nature has interposed a smooth muscle diaphragm between the endopelvic fascia and the levator ani muscle. Loss of elastic recoil and diminished sphincteric action are supplied by the presence of interwoven elastic tissue and smooth muscle fibers. The return to the normal postpartum state is assisted by the closely associated smooth muscle diaphragm which has the power of great extensibility. The fibromuscular diaphragm is not necessarily injured in normal childbirth. Dilatation of the uterus and cervical canal will slacken the tautness of the fibromuscular diaphragm, while return to the normal size of this viscus will renew the tension of the musculofascial diaphragm. By shifting of tissues and interplay of structures, marked excursion of dilatation and return to normal measures can take place in these associated diaphragms. These structural features are of great impor-

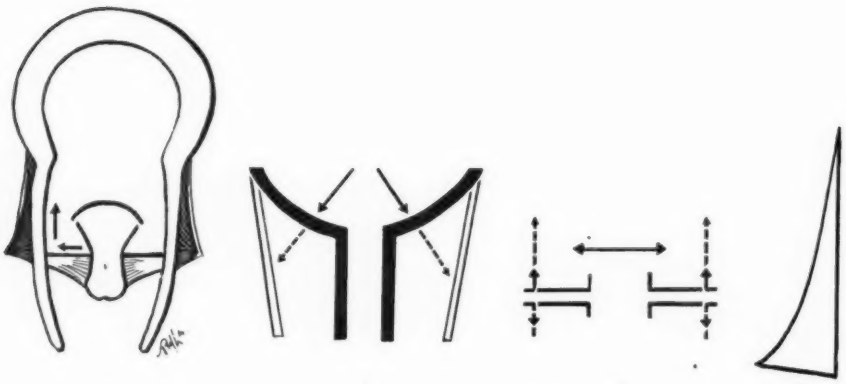

Fig. 2[1]. a, Center, structures at rest. Peripherally-L.U.S. stretched, vertically. L.L.C.U. stretched vertically, flattened peripherally. b, Oblique plane of L.A.M.D. converted into vertical one. c, Opening of U.G.D. indicated by arrows. d, Vertical stretching and peripheral flattening of L.L.C.U.

tance in the struggle for adaptability of spatial relationships that prevail between mother and child during parturition.

THE ENDOPELVIC FASCIAL DIAPHRAGM OR UPPER PELVIC FLOOR

If we look at a human embryo at about the 25th day, we find that the lower end of the abdomen is filled with a loose connective tissue through which the hind gut is passing dorsally and the allantois ventrally, these two structures meeting caudally in the cloaca. The coelom or the body cavity extends caudally for a short distance between the rectum and the allantois in front. Between the lower ectoderman wall of the abdominal cavity and the coelom is the subperitoneal pelvic space. In the embryo, this subperitoneal pelvic space is loosely packed with "embryonal connective tissue" and surrounds the as yet undifferentiated viscera. It really represents the as yet unseparated somatopleure and splanchopleure, the body cavity not having yet extended into this region to make a clear division between these two tissues. This tissue of course arises from the mesoderm and more especially from the mesenchyme of the middle germ layer.

In a 2 months' fetus (Fig. 4-31 mm. C.R.L.) a definite central condensation of mesoderm spans the fetal pelvis transversely enmeshing the lower third of the descending muellerian ducts. Their caudal extremity is thereby pulled caudally and medially, thus helping in their junction. This transverse mesodermal condensation is known as the "transverse mesodermal bar" by Fraser. In transverse section it can be seen to fan out into anterior, lateral, and posterior segments. In frontal section, it sends a caudal prolongation dividing the allantois from the rectum; thus separating the cloaca into the urogenital sinus anteriorly and the rectum posteriorly. This descending fascial prolongation terminates in the perineal body. At this stage, it is known as the urorectal septum. The anterior coronal segment is the anlagen of the cervicovesical fascia; the lateral condensation, the lateral ligaments of the cervix uteri (Mackenrodt); the posterior projection, the uterosacral ligaments; the caudal projection the rectovaginal septum. Thus the "transverse mesodermal bar" is the anlagen of the upper pelvic fascial floor.

In an eight month fetus the lateral ligaments of the cervix uteri (Mackenrodt) fuse with, and cover, the perimesium of the levator ani muscle and attaches solidly to the lateral vaginal walls.

In an adult multipara the endopelvic fascia reaches its greatest functional development, spanning the pelvis like a hammock, trans-

[1]Abbreviations throughout mean: L.L.C.U., lateral ligaments of the cervix uteri; L.A.M.D., levator ani muscular diaphragm; U.G.D., urogenital diaphragm; F.S., frontal section; U.S.F., uterosacral fibers; C.R., cervicorectal fibers; D., decussation fibers; B.L., broad ligament fibers; C.V., cervicovesical fibers; C.P., cervicopubic fibers.

versely from levator ani white line to levator ani white line, and anteroposteriorly from the symphysis pubis to the 2nd and 3rd sacral vertebrae, interrupted centrally by the urethra, cervix and vagina, and the rectum, the supravaginal cervix being the central pivotal attachment. A definite fascial fibrous capsule is present attached to the anterolateral and posterior supravaginal cervix (Fig. 5). This capsule is so arranged as to correspond to the functional demands of parturition and to the prerequisites of gynecology.

The physiological response to functional demands is greatest in parturition. Synchronously with the unfolding of the lower uterine segment a corresponding hypertrophy and hyperplasia of the endoplevic fascial structures takes place.

In the adult female topographically in coronal section the endopelvic fascia forms a diaphragm divided into anterior, lateral, and posterior segments. The anterior segment represents a platform situated beneath the bladder. Its fibers extend from the supravaginal fascial collar anteriorly to the symphysis pubis and to the anterior part of the levator ani white line. The lateral segment or condensation is known as the lateral ligament of the cervix uteri (Mackenrodt) and extends from the lateral margin of the supravaginal fascial collar to the levator ani white line. This is a well defined fascial ligamentous connective tissue capsule in the form of an inverted U (Fig. 6). It is attached to the anterior, superior, and posterior marginal walls of the supravaginal cervix. Laterally and inferiorly, this capsule is attached to the levator ani white line and to the levator ani fascia. It has anterior, superior, and posterior surfaces.

The superior surface presents large veins on its posterior aspect, while anteriorly the uterine artery is an individual entity, coursing above the fascial surface and marking the line of cleavage between this surface and the vesical fascia. Toward the lateral aspect, a reef of fascia extends obliquely from the posterior to the anterior leaf of the broad ligament above the capsule, deflecting the ureter in its lateral position.

At the extreme lateral aspect of this surface, the uterine artery crosses the ureter at a right angle. The ureter traverses the anterior margin of the surface in a preformed fascial groove (Figs. 5, 6, 7).

Fig. 3. Schematic representation of the various structures forming the pelvic floor. The lateral and posterior cervical ligaments L.L.C.U. (Mackenrodt), U.S.L., levator ani muscle, urogenital diaphragm, sphincteric group.

The anterior surface is the smallest of the three surfaces, because the levator ani muscle rises sharply in this region. The upper part of this surface fuses with the uterovaginal fascia giving the latter a wider "fixation span," while the lower part is attached to the fascia of the lateral vaginal wall. Caudally and laterally this surface is attached to the levator ani fascia.

The posterior surface is the largest of the three surface areas. It blends with the levator ani fascia. A foramen or gap is present between the ligament and the fascial fibers passing up from the levator to the vaginal fascia. A triangular space exists between the three surfaces (Figs. 3, 5, 6). The base of the triangular space faces caudally and laterally, being formed by the cranial fascia of the levator ani muscle.

In the normal adult this cavity contains areolar tissue and unstriped muscle. Smooth muscle fibers extending from the upper third of the vaginal wall are attached to the inferior aspect of the superior and posterior surfaces of the ligament (Fig. 8).

The posterior segment is the largest of the three areas, and its fascia the most attenuated because of the passage of the rectum. The most condensed fibers extend from the posterior inferior aspect of the supravaginal fascial collar, and terminate in the second and third sacral vertebrae. These fibers are known as the uterosacral ligaments. That space behind the cervix, bounded by the utersacral ligaments laterally and the rectum posteriorly is known as the pouch of Douglas (Fig. 5). This is the bottom of the abdominal cavity; here the fascial diaphragm is thinnest. In frontal section, descending caudally from the posterior margin of the supravaginal collar is a tonguelike reef of fascia extending between the posterior vaginal wall and the anterior rectal wall and terminating in the perineal body. This caudal prolongation is known as the rectovaginal septum.

THE SMOOTH MUSCLE DIAPHRAGM

During the last 3 months of fetal life, smooth muscle tissue exists in definite masses in the subperitoneal pelvic space. The arrangement of the tissue is identical with that in the adult, except that it is much less massive and the direction of the bands varies because of the difference between the positions of the pelvic organs in fetal and adult life. The smooth muscle tissue is not confined only to the areas immediately surrounding blood vessels and nerves. Most of it is made up of strands entirely independent of these structures. When they are reconstructed and viewed from the superior aspect, the direction of the fibers leads one to consider the tissue as an imperfect "diaphragm" of smooth muscle converging on the uterine cervix.

In the adult an imperfect smooth muscle diaphragm is present and embedded in fibrous tissue, lying between the endopelvic fascial diaphragm and the superior surface of the levator ani muscle. The smooth muscle bundles which constitute this diaphragm radiate from the uterus at the level of the internal os. The peripheral attachment of these bundles enables the tissue to be divided into three groups of fibers, anterior, lateral, and posterior groups.

The anterior fibers arise from the anterior and the anterolateral aspect of the cervix and are attached (a) to the posterior aspect of the os pubis, either directly or through the intermediary of fibrous bands, and (b) into the muscular coat of the bladder. The muscle fibers which make up this group can be subdivided into the following bundles: (a) the cervicovesical, (b) the cervicopubic, (c) the vesicovaginal, and (d) cervicovaginal (Fig. 9).

The lateral group The lateral group (which is identical with the lateral ligament of the cervix uteri—Mackenrodt) arises similarly from the lateral aspect of the cervix. They diverge and form a flattened fan of fibers which is attached by means of fibrous strands to the "arcus tendineus." This group is subdivided into an upper and lower bundle. From this group, slightly below level of internal os, fibers pass to the lateral vaginal fornix.

The posterior group The posterior group, also arising from the cervix, enters into the composition of the uterosacral ligaments or finds insertion into the rectal walls and rectovaginal septum. This group is subdivided as follows: (a) uterosacral fibers, (b) rectal fibers, (c) posterior vaginal fornix fibers, and (d) rectovaginal septum fibers.

Besides these distinctive strands enumerated, short fibers, like a fine platysma muscle, enter the anterior and posterior peritoneal layers of the broad ligament, from the corresponding uterine surfaces and end deep in the endothelium.

Dilatation of the connective tissue diaphragm, to the extent of permitting the passage of the fetal head, demands a great stretching of this poorly contractile tissue, which of itself could not assume its original dimensions as it contains little, if any, elastic tissue. The return to the normal postpartum state is assisted by the closely associated smooth muscle diaphragm which has the power of greater extensibility. The fibromuscular diaphragm is not necessarily injured in normal childbirth. Dilatation of the

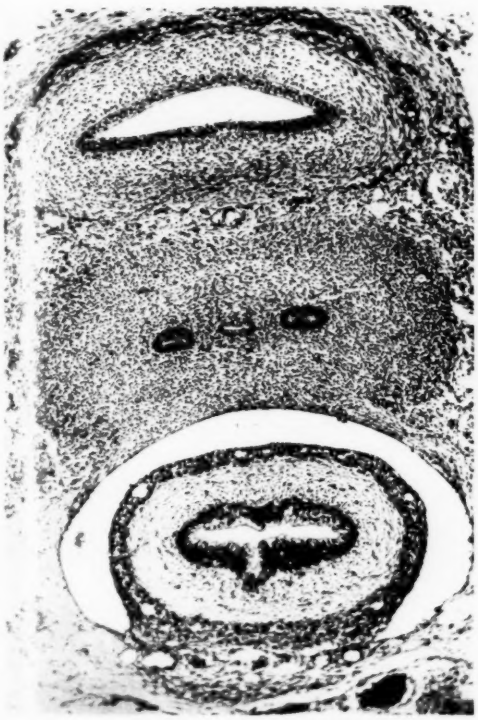

Fig. 4. (Fetus 31 mm. C.R.L.) Urogenital sinus in front. Transversus mesodermal bar containing the united mullerian ducts in the center and wolffian ducts on either side.

Fig. 5. Viewed from above. Showing the three surfaces of the lateral ligament. Like looking at the side of a funnel.

uterus and cervical canal will slacken the tautness of the fibromuscular diaphragm, while return to the normal size of this viscus will renew the tension of the musculofascial diaphragm.

THE LEVATOR ANI MUSCULAR DIAPHRAGM

This "ununiform" muscular plane spans the pelvis obliquely, stretching anteroposteriorly from the symphysis pubis to the sacrum and coccyx. Laterally from the levator ani white line, extending medially and caudally to the external sphincter of the anus, to the anococcygeal raphe, the sacrum, and coccyx.

The general sloping trend of the fibers medially and caudally give this muscle a somewhat "cup-shaped" appearance, with a trough-like exit beneath the symphysis pubis —where the medial arms of the pubococcygeal segment enclose two clefts. An anterior one, the urethrovaginal, and an anal one, posterior to the perineal body. While the origin of this diaphragm is fixed to bone, particularly its anterior and posterior segments, its insertion is mobile, the significance of this fact increases with parturition.

From an obstetrical viewpoint the levator ani muscular diaphragm on each side consists of three segments—an anterior or pubococcygeal, a middle or iliococcygeal, and a posterior or ischiococcygeal. These bifurcated muscles take an extensive origin from bone and fascia.

The anterior segment consists of the pubococcygeus muscle, by far the most important of the three segments. It forms the largest, strongest, thickest, and most important part of the pelvic floor. Its fibers have a bony origin from the posterior wall of the symphysis pubis beneath the levator ani white line; and

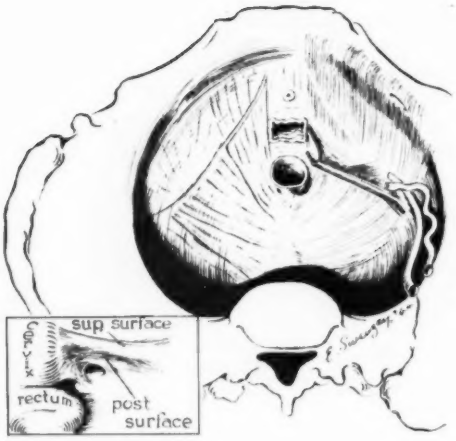

Fig. 6. Semidiagrammatic representation of pelvic floor with right lateral cervical ligament shown in position. (On the left side the fascia has been removed to show the underlying muscles.) At the lateral end of this ligament the uterine artery can be seen crossing the ureter. At the medial end of the ligament the inverted U-shaped outline is well shown. The small insert shows the ligament from behind. Note the hiatus at the lower border of the posterior surface.

from the arcus tendineus in front of the obturator canal. From this origin its fibers sweep backward as three distinct bands, the most medial fibers form a U loop around the vagina and are inserted into the "central point" o the perineum with firm attachment to th cranial leaf of the urogenital diaphragm. These fibers constitute the "pubovaginalis." A thin bundle is confluent with the urethrali muscle.

The intermediate fibers resemble a horse-shoe attached by its anterior extremities to the pubis and encircling the rectum behind, forming a U loop around the anorectal junction. These fibers constitute the puborectalis or sling muscle, which slings the anal canal up to the symphysis pubis. Some fibers from this bundle insert into the anococcygeal raphe.

The most lateral fibers have a Y shaped insertion into the anococcygeal raphe—the margins and ventral surface of the coccyx. This muscle forms a sphincter for the vagina and anal canal, and also increases the anorectal angulation. It gives off accessory fibers to the urethralis muscle, which act as an accessory sphincter of the urethra.

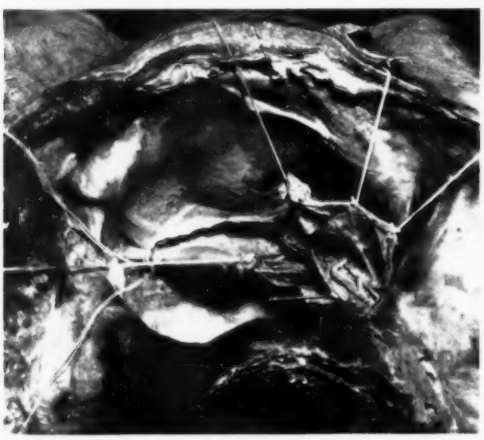

Fig. 7. Dissection. Lateral ligament of cervix uteri (Mackenrodt) viewed from above presenting superior surface. (Probe under ureter.)

Fig. 8. Dissection. Seen directly from above. Later cervical ligament (Mackenrodt). Uterus and uterine arte deflected posteriorly. Ureter in position. *1*, Superior su face; *2*, smooth muscle fibers; *3*, cervicovesical junctio

The iliococcygeus lies posterior to, and on a deeper plane than, the pubococcygeus. Viewing the pelvic floor from above (Figs. 3, 5, 6, 10) actually it is more superficial. It is attached to the arcus tendineus behind the obturator canal and is inserted into the anococcygeal body and into the margins of the coccyx, lateral and caudal to the fibers of the pubococcygeus. Occasionally this muscle retains its primitive origin from the pelvic brim. In lower animals it has a flat tendinous origin from the iliopectineal line. Since it has lost its original purpose in man it is poorly developed, and has slipped lower down on the pelvic wall. Its fascial point of attachment has become elongated, therefore, so that the fibers of origin of the muscle do not, except in a few instances, extend to such a degree as the iliopectineal line.

In most cases in the dissecting room, muscle fibers can be demonstrated only at a considerable distance from the point of origin of this muscle.

The elongated and thinned out "aponeurosis" of the iliococcygeus muscle is seen to be intimately fused with the sheath of the obturator internus muscle.

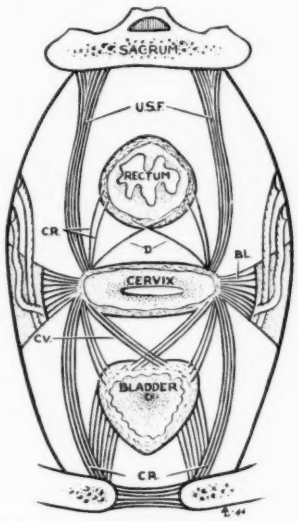

Fig. 9. Schematic transverse section of smooth muscle diaphragm. *U.S.F.*, Uterosacral fibers; *C.R.*, cervicorectal fibers; *D.*, decussation fibers; *B.L.*, broad ligament fibers; *C.V.*, cervico vesical fibers; *C.P.*, cervicopubic fibers.

Fig. 10. Semidiagrammatic mesial section of pelvis, showing the mutual relationships of the components of the pelvic diaphragm. Notice especially the upper and lower leaves of the urogenital diaphragm.

The fusion of the remains of the aponeurosis of the iliococcygeus with the fascial covering of the obturator internus muscle forms a composite sheath of fascia, the so called obturator fascia. The line of fusion between these two fasciae is of considerable clinical importance, in that it defines the upper limit of the ischiorectal fossa.

The so called "white line" does not accurately indicate the upper limit of the iliococcygeus muscle but rather an arrangement of its fascial investment. This fascia is subject to tension between two fixed points and has become condensed. In this instance the fascial fibers of the sheath of the levator ani form a narrow band popularly referred to as the "levator ani white line," which extends from its point of attachment on the posterior aspect of the pubis to the spine of the ischium. The white line, therefore, appears to cross the

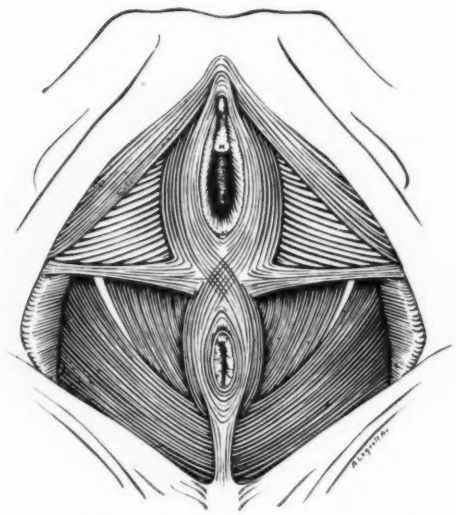

Fig. 11. Schematic representation of the sphincteric muscular group of the pelvic floor.

pubococcygeus muscle because unlike the iliococcygeus, the former has not descended. The white line in some cases is found separated by some little distance from the pelvic wall and when this is so a pouch—the "hiatus of Schwalbe"—filled with fat, exists between the two.

The D shaped opening of the anus, previous to expulsion of the fetal head, is due to extension of the fibers of the puborectalis and iliococcygeus which are inserted into the anococcygeal raphe.

The ischiococcygeus with the piriformis forms the muscular upholstery which closes the posterior part of the pelvic outlet. Posteriorly and caudally it is reinforced by the sacrotuberous ligament (great sacrosciatic ligament). This triangular muscle is set at almost a right angular plane to the iliococcygeus. It arises from the apex of the ischial spine and is inserted fan-shapedwise into the lateral border of the sacrum and into the lateral margins of the coccygeal bodies, conjointly with the iliococcygeus muscle.

The individual muscle sections of the pelvic diaphragm do not by any means form a uniform sheath in one plane, but overlap one another posteriorly where they join and interdigitate with the muscle fibers of the other side. By this means the part of the diaphragm posterior to the rectum is clearly strengthened.

Morphology. In pronograde animals there are three caudal muscles; the pubococcygeus, arising from the body of the pubis, the iliococcygeus arising from the pelvic brim, both of which are tail depressors, and the ischiococcygeus, a lateral flexor of the tail arising from the ischial spine. With the disappearance of the tail in man and the assumption of the upright position, the tail muscles take over new duties and form a pelvic floor for the support of the pelvic viscera. The pubococcygeus and the ischiococcygeus muscles retain their primitive origins, but the iliococcygeus loses its attachment to the pelvic brim and gains a new attachment to the lateral pelvic wall at the arcus tendineus. While the caudal muscles gain extensive new insertions into the pelvic floor, they still retain their original insertion into the coccyx, which is the rudimentary tail. Thus, while the levator ani muscular diaphragm contributes to the support of the viscera, the muscles which constitute it are derived from the flexors and abductors of caudal end of vertebral column.

THE UROGENITAL DIAPHRAGM

The urogenital diaphragm is a relatively inelastic double-leafed fascial envelope, extending between the ascending pubic rami and beneath the subpubic arch, to whose margins it is firmly attached (Figs. 3, 10, 13 to 18). It closes over the perineal triangle, while its so called free margin extends between the ischial tuberosities, demarcating the posterior boundary line of the perineal triangle. It is perforated by the dorsal vein of the clitoris, the urethra, and vagina. It contains the pudendal vessels and nerves and the membraneous urethra, the sphincter urethrae and transversus perinei profundus muscles. This latter muscle is supportive to the vaginal wall.

The pubococcygeal segment of the levator ani muscle plays on its cranial fascia into which fibers of this muscle find a firm attachment. Thus the integrity of this fascial leaf prevents within certain limits the separation of the pubococcygeal segment. The wedge-shaped, anteriorly directed diverticulum of the ischiorectal fossa extends between the

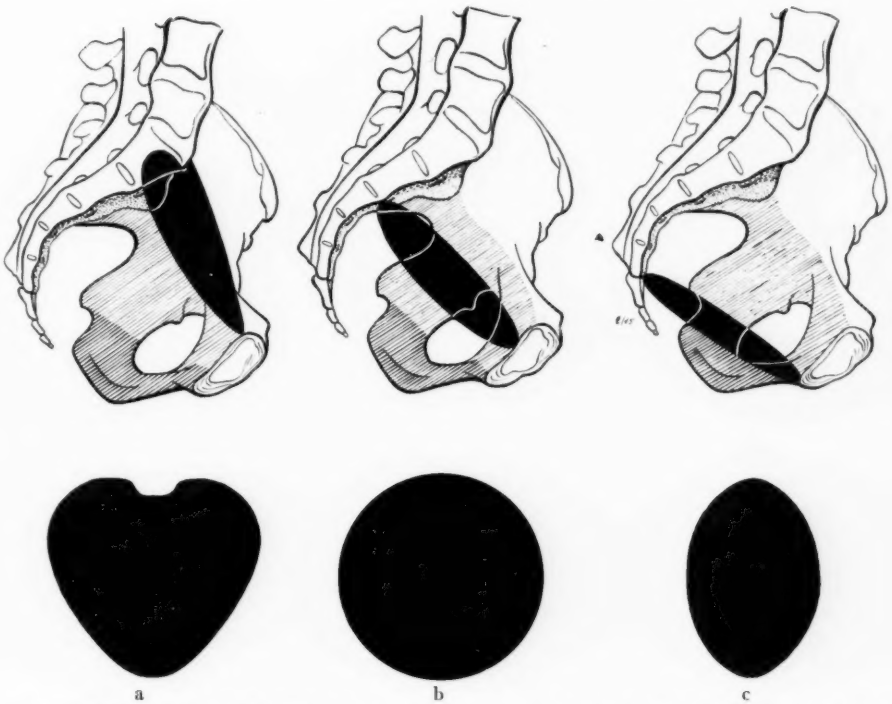

Fig. 12. (Silhouettes) a, Android inlet; b, midpelvic plane, round; c, level of ischial spines and plane of pelvic floor, spheroidal.

pubococcygeus muscle and its cranial fascia. Its caudal fascia gives attachment to the sphincteric vulval musculature. With the body in the erect position, the urogenital diaphragm, like the os pubis and its rami, is in a horizontal plane, so that support of the pelvic viscera falls upon these structures.

THE SPHINCTERIC MUSCULAR DIAPHRAGM

While this group offers some supportive action it is primarily sphincteric in contradistinction to the levator ani muscular diaphragm which is primarily supportive and only secondarily sphincteric to the pelvic viscera. It forms sphincters for the openings of the canals which perforate the pelvic floor to reach the exterior. It is derived from the primitive sphincter cloacae, a primitive muscular ring surrounding the cloaca, which is partly attached to the bones at the pelvic outlet.

During the course of the development of the genitourinary organs a cloacal aperture exists till about the 5th week, and a sphincter muscle is arranged about it—the primitive sphincter cloacae. About this time a caudal prolongation of the transverse mesodermal bar takes place dividing the cloaca into two parts, a dorsal or anal, and a ventral or urogenital, and coincident with this change the sphincter cloacae becomes divided into dorsal and ventral divisions, the former surrounding the anal aperture and constituting the sphincter ani externus, the ventral surrounding the urogenital sinus. It is from the urogenital division that the bulbocavernosus, the ischiocavernosus, the transversus perinei and the sphincter urethralis muscles develop (Fig. 11).

ACCESSORY STRUCTURES

Perineal body. The perineal body or central tendon of the perineum is a triangular wedge

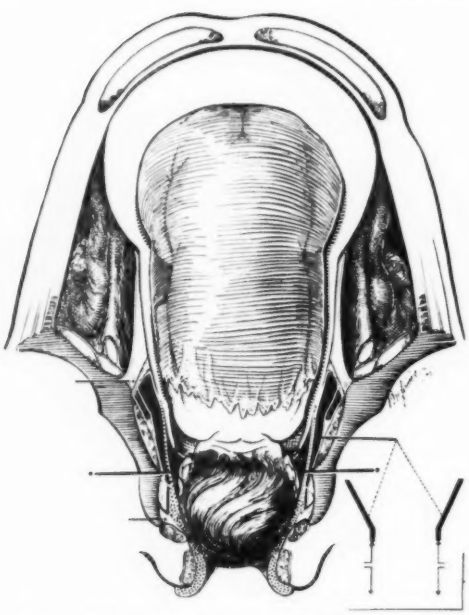

Fig. 13. F.S. Internal rotation completed. Levator ani muscular diaphragm funnelled. Head in axis of pelvic outlet. Urogenital diaphragm opening. Upper leaf being pulled upward by dilatation of vagina and pubococcygeal segment. Lower leaf being pushed downward by descending head. Coiffure of hair indicating direction of rotation.

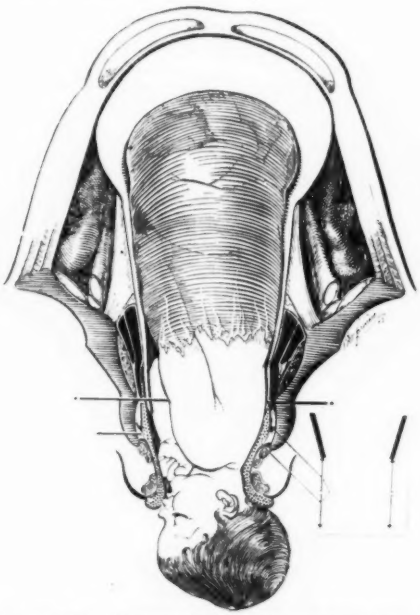

Fig. 14. F.S. Uterovaginal canal converted into one continuous hiatus. Lateral ligaments of the cervix uteri flattened peripherally and stretched vertically to their maximum. Levator ani muscular diaphragm changed to vertical plane. Urogenital diaphragm widely opened. External rotation completed.

of tissue whose base is represented by the skin surface existing between the posterior commissure of the vagina and the anterior margin of the anus. Its apex is demarcated by the line of juxtaposition of the posterior vaginal wall and the anterior rectal wall. It is made up of fat, connective tissue, voluntary and smooth muscle fibers. Laterally it receives fascial lamella from the perivaginal and perirectal fascia. The lamellar layer of the rectovaginal septum extending from the supravaginal cervix serves as a veil suspending its apex. This structure is analogous to the hub of a wheel or the ring of a parachute, into which is inserted each one of the diaphragms constituting the pelvic floor. It has been popularly called the tendo achillis of the perineum. The perineal body is the "keystone" of support to each of the various diaphragms constituting the pelvic floor. Injury to the perineal body is reflected in each of these structures. The baby has to come down the uterovaginal canal to make its exit. The vulva at the anterior end contains the bony undistensible platform. However, the symphysis pubis opens slightly and the coccyx is displaced downward and backward. The visceral structures with their fascial attachments move upward, the muscular segment, the levator ani moves downward and backward and both segments are canalized. The pelvic floor has to be opened and closed; to be opened, it is displaced backward and downward. If it is damaged, it cannot be completely closed. A torn and damaged perineal body is going to prevent return to integrity.

Gluteus maximus muscle. The levator ani muscular diaphragm receives support from the two gluteus maximus muscles. These muscles are a source of strength capable of presenting great counterpressure to the powerful muscles of the ventral wall and the respiratory diaphragm. The lower medial fibers of the muscles pass downward and backward from the

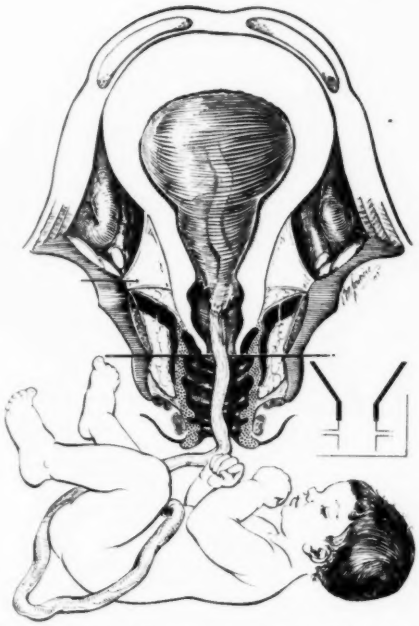

Fig. 15. F.S. Baby expelled. Lower uterine segment fibers regaining contractility and its canal diminishing in volume. Lateral ligaments of the cervix uteri assuming axial arrangement. Levator ani muscular diaphragm fibers regaining oblique plane. Urogenital diaphragm closing.

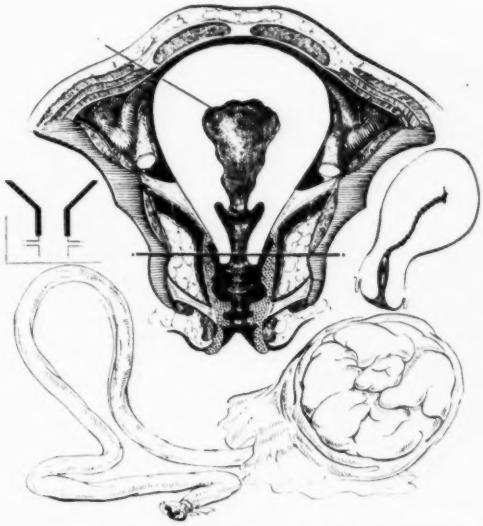

Fig. 16. F.S. Restitution. Placenta expelled. Cervix withdrawn cranially to level of ischial spines. Lateral ligaments of the cervix uteri in normal axial pregravid plane. Levator ani muscular diaphragm in oblique plane. Urogenital diaphragm closed.

coccyx, separated from each other by an angle of 30 degrees and connected by tough, intervening connective tissue. They underlie each ischiorectal fossa and support the pelvic diaphragm very powerfully through the pad of fat which fills these fossae. The fat pad in the ischiorectal fossa is made up of small masses of fat with powerful strings of connective tissue fibers intervening with one another and connected with the walls of the fossa, with the perimysium externum of the internal obturator and gluteus maximus muscles and with the caudal fascia of the urogenital diaphragm, which limits the ischiorectal fossa anteriorly. The fat pad lies under the levator ani muscular diaphragm throughout its extent and so forms a cushionlike support which, though soft and pliable, transmits to the levator ani muscular diaphragm all the strength and security given it by the gluteus maximus muscles and the powerful urogenital diaphragm. These offer real strength and support to the levator ani muscular diaphragm. The fat pad is continuous with the fat of the adjacent superficial fascia. The superficial fat of perineum and the apposition of medial aspects of the thighs also act as accessory, supportive structures.

THE COURSE OF PARTURITION

The bony pelvis is a funnel-shaped bony cage with a bend resembling the elbow of a stovepipe. Its gently sloping walls and muscular upholstery offer deflecting surfaces to the fetal head during parturition. It possesses a bore, similar to that of a turbine, or rifle—the fetus representing the bullet which, passing through, must make certain turns in order to accommodate itself to the unequal bore of the pelvis.

Previous to the onset of labor the fetal head rides at ease in the "military position" above the obstetrical inlet, the posterior quadrant of which passes through the body of the first sacral vertebra, the longitudinal axis of the fetal ovoid being parallel with the vertebral column of the mother (Figs. 17, 18).

With labor established, the fetal head is first "jockeyed" into one of the oblique diameters

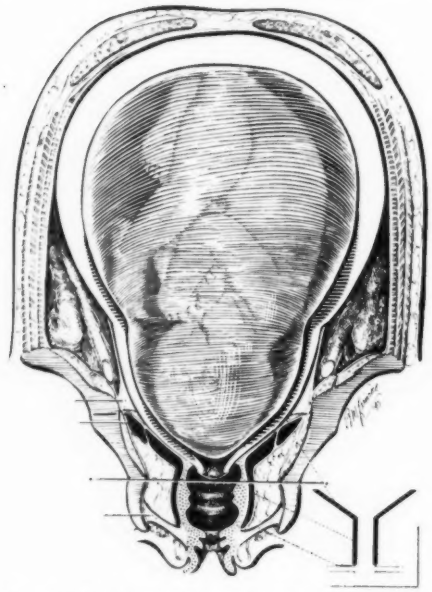

Fig. 17. F.S. Schematic frontal section slightly anterior to bisected anteroposterior diameter of pelvic inlet. Labor established. Head "centered" in axis of inlet. Membranes intact. Lower uterine segment unfolding. External os dilating. Lateral ligaments of the cervix uteri flattening peripherally and elongating vertically. Levator ani muscular diaphragm receiving pressure from the fetal head. Urogenital diaphragm intact.

Fig. 18. F.S. Lower uterine segment further unfolded. Membranes bulging. External os further dilated. Peripheral and vertical stretching of the lateral ligaments of the cervix uteri. Levator ani muscular diaphragm being funnelled. Vaginal fornices pulled upward. Urogenital diaphragm intact.

of the pelvic inlet, usually the right, this being the relatively larger of the two diameters, its sagittal suture passing from the oblique to the transverse diameter of the obstetrical inlet. The passenger is then propelled along the road of birth, the axis of which is backward and downward to the ischial spines (Figs. 12c, 19) the area of least dimensions, which is also the plane of origin of the pelvic floor; then forward and slightly upward through the pelvic outlet. The bore of the road of birth causes the passenger to make three turns during its voyage, one at the inlet, a second at the ischial spines (internal rotation), and a third (external rotation) which is on the balcony of soft parts beyond the bony pelvis (Figs. 12, 14).

When the descending head strikes the pelvic floor, the muscular segments react by increased oscillations, thus temporarily assuming a horizontal plane. When the muscular resistance is overcome, a vertical plane is assumed and the levator ani muscle is said to be "funnelled."

The levator ani muscular segments are funnelled from behind forward. The ischiococcygeus is the first to receive the impact of the fetal head, but the head is preceded by the membranes filled with fluid forming a wedge whose narrow lower end slips into the vagina and really transfers most of the pressure onto the front of the pubococcygeus just where it passes into the perineal body. Thus the anococcygeal raphe is pushed down at its anterior end until it becomes ventral, and the ischiococcygeus, which is set at almost a right angular plane to the iliococcygeus, assumes a vertical plane and acts as a deflecting surface to the descending head. With the propelling force of the contracting upper uterine segment, the head is deflected downward and forward onto the fibers of the iliococcygeus

Fig. 19. F.S. Membranes ruptured. Descent of head to ischial spines. Sagittal suture is in oblique plane. Further flattening and stretching of the lateral ligaments of the cervix uteri. Fibers of the levator ani muscular diaphragm changing from oblique to vertical direction. Pull being exerted on upper leaf of the urogenital diaphragm.

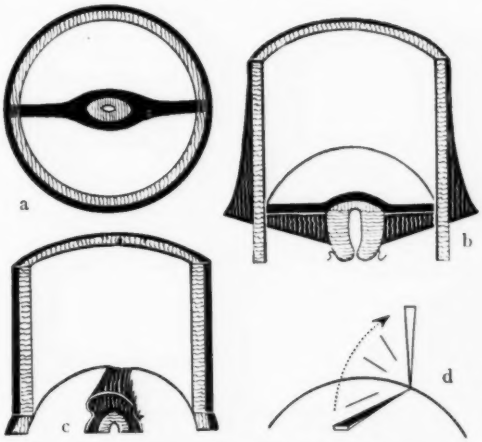

Fig. 20. a, Transverse section of cervix and supravaginal fascia. Center, cervix. Cervix represented by light wavy lines. Fascial collar by heavy dark lines. b, Frontal section. Effaced lower uterine segment and adjacent elongated fascia in vertical plane. Peripherally dilated in transverse plane. c, Sagittal section. Center, cervix and lateral ligament of the cervix uteri at rest. Periphery, in dilatation. d, Action. Diagram illustrating flattening and elongation of lateral ligaments of the cervix uteri. These ligaments flatten peripherally with dilatation of the lower uterine segment and elongate with its vertical stretching.

muscle. The fibers of this muscle slope medially and caudally; their resistance is soon overcome and the head is then shunted on to the pubococcygeal segment, which is stretched anteroposteriorly and peripherally. As the peripheral dilatation of its fibers takes place, the urogenital diaphragm is opened. The adjacent cranial leaf of the urogenital diaphragm turns upward on the sides of the vagina and has attached to it the fibers of the pubococcygeal muscle. Thus, as the vagina dilates and the pubococcygeus is dilated peripherally the cranial leaf of the diaphragm is pulled upward. The caudal diaphragmatic leaf is pushed downward as the head is propelled along the axis of the pelvic outlet (Figs. 10, 13, 14). The transversus perineii profundus muscle is flattened peripherally and stretched vertically, its fibers being dispersed between the upper and lower fascial leaves. The rectovaginal septal fibers are stretched peripherally and longitudinally. This septum can sometimes be seen being pushed in front of the descending head, if stretched beyond its elastic capacity, this structure tears, either vertically or transversely, severing its continuity with the perineal body.

As the sphincteric group of muscles are dilated they are converted into a short muscular tube along the axis of the pelvic outlet. Their stretched fibers extend beyond the bony framework. When the biparietal diameter of the fetal head reaches the transverse diameter of the pelvic outlet, the perineum bulges for a distance of 1.5 to 2 inches. Coincident with this bulging, or "crowning," the coccyx and anococcygeal raphe are being displaced downward and backward. The posterior fibers of the external sphincter, which are attached to the anococcygeal raphe, are stretched and pull the anus open in a D-shaped fashion. At this moment the uterovaginal canal is converted into one continuous hiatus (Figs. 1, 14). The lateral ligaments of the cervix uteri are flattened peripherally and stretched vertically. The smooth muscle diaphragm is dilated spherically and the leva-

tor ani muscular diaphragm changed from an oblique to a vertical plane. The urogenital diaphragm is opened and the sphincteric diaphragm dilated spherically, followed by dilatation of Colles' fascia and the skin surface.

While the lower uterine segment starts to unfold at the fourth month of intrauterine life, it is only fully developed as a mechanical product of labor. Synchronously with the unfolding of the lower uterine segment, a hypertrophy and a hyperplasia of the supracervical fascial collar takes place. As the lower uterine segment widens and elongates, the fascial collar correspondingly follows it. With the establishment of labor the lateral ligaments of the cervix uteri have grown and stretched considerably in size so that, metaphorically, they may be likened to the stretching of a rubber to that of a rubber boot. At the moment of expulsion of the fetal head, the uterovaginal canal is converted into one continuous hiatus, the lateral ligaments of the cervix uteri are flattened peripherally and elongated vertically. When the baby is expelled, the lower uterine segment regains its contractility and its calibre is diminished with a corresponding contractility and reduction in size of the stretched endopelvic fascial structures. The lateral ligaments of the cervix uteri contract in their vertical length and regain their axial arrangement in the horizontal plane (Fig. 15).

With the expulsion of the placenta, the caliber of the lower uterine segment is further reduced. The cervix rises to the ischial spines. The lateral ligaments of the cervix uteri assume their pregravid axial arrangement (Fig. 16). The anterior and posterior fundal walls are in apposition, being separated only by filamentous bands of fibrin and blood clot. Further involution follows provided the anatomical integrity of the supporting pelvic structures has been maintained. The fascial diaphragm is likewise favorably affected by involution or unfavorably affected by subinvolution. Trauma or infection of the isthmicocervical canal will likewise affect the adjacent fascial supports. Should the fascial and levator ani muscular diaphragms be traumatized and unrepaired, prolapse will inevitably follow.

THE CLINICAL SIGNIFICANCE OF THE PELVIC FASCIA IN OBSTETRICS

The endopelvic fascia—as an extensive fixation apparatus moors the uterus to the levator ani white line and to the pelvic floor.

The lower uterine segment and its fascial supports represent an active force in determining the axis along which the fetal head must descend through the pelvis.

The fascial attachments of the lower pole of the uterus influence the fetal ovoid in its descent through the pelvis.

The fascial supports of the uterus have received many names. Among others, the following designated titles have been applied: the parametrium (Virchow), the cardinal ligaments (Kock), the vascular sheath (Charpy), the hypogastric sheath (Pierre Delbet), the uteroiliac process (Savage), ligamentum lata, tunica vasorum uteri (Merkel), ligamentum transversale colli (Mackenrodt), the sustentacular apparatus (Bonney), the lateral cervicopelvic ligaments, the upper pelvic floor (Polls).

The anglicized version, namely, "the lateral ligament of the cervix uteri" is a more meaningful and purposeful terminology, and in keeping with the principles accepted at Basle, in 1895, by the Anatomical Society.

Because of its fixation to the elastic levator ani white line laterally, and to the supravaginal cervix medially, with the formation of the lower uterine segment this fascial diaphragm hugs the lower uterine segment, and is elongated in a cranial direction assuming somewhat the topographical outline of an inverted expanding funnel or inverted Medici collar. Its weakest point is posteriorly between the uterosacral ligaments where the fascial collar is thinnest. Metaphorically, it may be said to be stretched from the "size of a rubber to that of a rubber-boot."

The lower uterine segment is formed from the body of the uterus, the isthmus and cervix. In full development it is a mechanical product of labor, being the passive or accordionated portion of the cervicouterine canal. The contraction ring not only marks the line of demarcation between the contractile part of the uterus and the lower uterine segment but also delineates the cranial attachment of the

fascial aponeurosis to the lower uterine segment. Beneath the line of attachment of this fascial ring the passive lower uterine segment has great freedom of movement. When fully developed the lower uterine segment may become as thin as a "gold leaf" and of itself could offer little guidance to the lower presenting fetal pole, in its passage through the pelvic axis. However, because of the intimate attachment of this durable stretched sail-like fascia to the lower uterine segment, the lower uterine segment and its juxtaposed fascia "conjointly" play an important physiological rôle in guiding the fetal pole into and through the pelvic axis during parturition.

At the brim of the pelvis it may tilt the child's head toward the symphysis pubis in the fore-pelvis, or carry it backward toward the center of the pelvis, or direct it to the posterior pelvis, its maximum guiding influence becoming more evident only after definite dilation of the cervix has been accomplished.

When the biparietal diameter of the fetal head is in the fully dilated cervix, the guiding influence of the lower uterine segment and its fascial supporting structures are entirely passive; the lower uterine segment at this stage is extremely thinned while the fascial collar is shortened and thickened. Both structures have conjointly helped the fetal head to this level; their function is now temporarily suspended. The longitudinal axis of the fetal ovoid does not always correspond to the axis of the pelvic canal but, by the "check" of the fascial collar it may be deflected into the pelvic axis.

During the first stage of labor, depending on the direction through which the fetal head is guided by the soft parts, it may be deflected into either (a) the fore-pelvis with the anterolateral aspect of the head close to the symphysis pubis, or (b) with the head centrated in the pelvis (theoretically equidistant from the pubis and sacrum), or (c) into the posterior pelvis. Diversion of the head into one of these avenues of descent is accomplished by the conjoined action of the lower uterine segment plus the adjacent fascial diaphragm, both acting as a deflecting surface. The longitudinal fetal axis is driven downward by the upper contractile uterine segment.

The lateral and caudal attachments of this fascial diaphragm are far reaching. They act as fixation spans. Laterally the fascial aponeurosis is continuous with the hypogastric sheath. The caudal extensions of this fascial aponeurosis extend from the posterior wall of the symphysis pubis and from the levator ani white line to the ischial spine, and to the periphery of the great sacrosciatic notch: to the vaginal fascia in its lateral aspect and to the periphery of the urogenital hiatus. These extensions give a wide perch to this tensile, pliable fascial aponeurosis, empowering it to moor the uterus not only to the levator ani white line but to the composite structure of the pelvic floor and to the bony pelvic canal as well.

After delivery of the placenta the vaginal introitus usually appears pouting. Should the uterus be lifted upward the vaginal introitus will immediately become inverted, presenting tangible proof of the caudal terminal attachment of the endopelvic fascia to the lateral fascial aponeurosis of the vaginal wall.

The axis of the lower uterine segment must be influenced by its fascial attachments to the levator ani white line and to the bony pelvis. Variations in this axis could, by such attachments, exert a profound influence on the mechanism of labor.

This elongated fascial collar in juxtaposition to the stretching and thinned lower uterine segment acts as a check in guiding the lower pole of the fetal ovoid into the pelvic brim. Deficiencies in this fascial sheath are reflected in maladjustments of the presenting part. Shortening of one or more segments (due to trauma, developmental, or infective agents) will deflect the head at the inlet from the pelvic axis to one or other pelvic quadrants, i.e., to the fore-pelvis or posterior pelvis —leading to delay of engagement and asynclitism.

AN EVALUATION OF CERTAIN DRUGS USED TO MAINTAIN BLOOD PRESSURE DURING SPINAL ANESTHESIA

Comparison of Ephedrine, Paredrine, Pitressin-Ephedrine and Methedrine in 2500 Cases

ROBERT D. DRIPPS, M.D., and MARGERY VAN N. DEMING, M.D.,
Philadelphia, Pennsylvania

THE administration of a pressor drug prior to the onset of spinal anesthesia has become almost routine. Various sympathomimetic substances have been employed in an effort to maintain blood pressure during this type of anesthesia, the list including practically every vasoconstricting agent known to pharmacology. With such a large group of drugs available it is difficult to select a particular one and be reasonably certain that the best has been chosen. It is evident, therefore, that definite criteria should be established for such a selection and that large series of controlled cases be analyzed so that new drugs can be critically compared to those in common use today. Certain questions demand answering: first, what can be expected to happen to blood pressure if pressor drugs are not used; second, is there one particular drug which is more effective in maintaining circulatory adequacy during spinal anesthesia; and third, are there side-actions of some of these drugs which make their use less desirable despite a proved ability to sustain blood pressure?

In an effort to answer some of these questions a study has been made of 2500 patients to whom spinal anesthesia was administered. This series was divided into groups of 500 cases as nearly alike as possible according to age, type of operation, physical condition, and type of anesthetic agent. The same group of surgeons and anesthetists functioned throughout the study and preoperative preparation of the patients remained essentially unchanged during the investigation. Five hundred patients received no pressor drug, and a group of 500 each received ephedrine, paredrine, a combination of pitressin and ephedrine, and methedrine. These four drugs or combinations were selected for study because of the widespread use of ephedrine prior to spinal anesthesia (Ockerblad and Dillon, 1927; Ferguson and North, 1932; Lundy, 1942), the utility of pitressin-ephedrine as described by Chaikoff (1940), and the good results obtained with paredrine (Altschule and Gilman, 1939; Nathanson, et al., 1942). Methedrine was chosen on the basis of the work of Dodd and Prescott (1943) which suggested that the prolonged action of this drug might constitute a real advance in prophylaxis. The course of the blood pressure subsequent to the administration of these various pressor drugs has been analyzed statistically from a number of viewpoints.

The cases comprising this series were unselected. Every patient given spinal anesthesia in this hospital was included, and as soon as 500 consecutive patients had received a particular drug, another drug was substituted and the next 500 cases collected. This continued until the entire series of 2,500 patients had been observed. Because of the nature of the surgical admissions the types of cases are remarkably constant throughout the year and each group of 500 patients represents a fairly predictable series as far as operative procedures are concerned. Thus, when the groups are divided according to type of operation the distribution is as shown in Table I.

From the Department of Anesthesia, Hospital of the University of Pennsylvania, and the Harrison Department of Surgical Research, University of Pennsylvania School of Medicine.

TABLE I.—DISTRIBUTION

	Methedrine	Paredrine	Ephedrine	Pitressin and ephedrine	None
Inguinal and perineal	179	163	166	158	220
Lower extremity	36	40	38	33	53
Lower abdominal	170	171	183	186	155
Upper abdominal	87	90	88	92	50
Kidney	28	36	25	31	22
Total	500	500	500	500	500

TABLE II

	Methedrine	Paredrine	Ephedrine	Pitressin and ephedrine	None
Procaine	221	201	206	179	199
Pontocaine	230	242	237	252	269
Nupercaine	49	57	57	69	32
Total	500	500	500	500	500

An effort was also made to avoid unbalancing any particular group as far as an anesthetic agent was concerned. Procaine hydrochloride crystals dissolved in cerebrospinal fluid to form a 2.5 to 5 per cent solution, 1 per cent pontocaine solution combined with varying amounts of dextrose and a 1:1500 solution of nupercaine hydrochloride were the only drugs used. Their distribution according to groups was as shown in Table II.

STATISTICAL ANALYSES

In analyzing the results it was frequently necessary to determine whether the different types of treatment produced results which were significantly different. This was accomplished by calculating the statistic *t* for data of the graded type, i.e., change in blood pressure expressed as a percentage of the initial value. This statistic takes into account (1) the difference between the means of each of the two groups being compared, (2) the degree of variation within each group, and (3) the number of observations per group. If the tables for the distribution of *t* indicate that the particular value of *t* obtained is so large that it could be expected from chance alone only once in 20 times, it is conventional to assume that the difference between the two groups of data is so great that it is responsible for the large *t* value and therefore significant. If the *t* value is so large that it could be expected by chance alone only once in 100 times, the difference is considered highly significant. The calculation of *t* is described in such standard texts on statistics as that by R. A. Fisher.

Fisher also describes the use of chi-square, which is a statistic to be used when the data are of the all-or-none type as is the case when results are classified as being either below or above a 25 per cent fall in blood pressure. This test answers the question of whether the proportion of the cases above the 25 per cent level to those below the 25 per cent level is significantly different in the two groups being compared. Here also, as with the *t* test, if the chi-square value obtained could be expected from chance alone only once in 20 times, the two groups of data may be considered significantly different. If the odds are one in 100 the difference is highly significant.

DOSAGE

Only one dosage of the various pressor drugs was used with the exception of methedrine where either 20 or 30 milligrams was administered. Statistical analysis of the results showed no significant difference between the response to 20 and 30 milligrams of methedrine. The mean percentage fall in blood pressure was 2.91 per cent for 20 milligrams and 3.06 per cent for 30 milligrams, $t = 0.065$, a value showing no significant difference between these means. It was, therefore, deemed justifiable to group together all data on methedrine regardless of which dosage was used.

Ephedrine sulfate was administered in 50 milligram doses; paredrine in 10 milligram doses, and the combination of pitressin-ephedrine included 10 units of pitressin and 50 milligrams ephedrine. All drugs were injected into the erector spinae muscles 3 to 10 minutes prior to the injection of the anesthetic agent into the subarachnoid space.

BLOOD PRESSURE DETERMINATIONS

Blood pressure was determined by auscultation over the brachial artery. Control values were those taken after the patient had received preoperative medication and had been

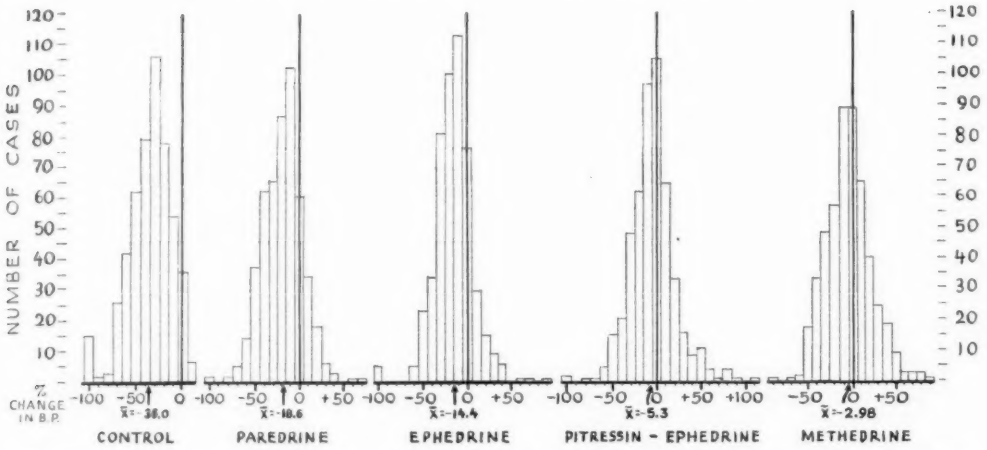

Fig. 1. Frequency distribution of maximum per cent change in blood pressure from preoperative level during operations under spinal anesthesia. Each pressor drug group and the control group (no pressor drug) includes 500 cases, a total of 2,500 cases. The height of each bar represents the number of cases having the percentage change in blood pressure indicated along the horizontal axis. Each bar represents a range of 10 per cent change in blood pressure; i.e., 5 to −4 per cent, −5 to −14 per cent, etc. The heavy vertical line indicates the position of no change in blood pressure from the initial level. The arrow points to the average (mean) per cent change in blood pressure for the group, designated by the symbol $\bar{X}$. Note the progressive shift in the mean per cent change in blood pressure and the decrease in number of cases having a fall in blood pressure in the groups to the right of the control group. This shift in the mean per cent change clearly demonstrates the value of pressor drugs, and their relative effectiveness in minimizing the tendency of spinal anesthetics to bring about a fall in blood pressure.

brought to the operating room. After administration of the anesthetic, blood pressure readings were taken at 5 minute intervals or less. No attempt was made to differentiate between the hypotension associated with spinal anesthesia alone, or that related to traction reflexes, surgical shock, or hemorrhage. It was felt that the series was large enough to be treated in this fashion. Blood pressure changes obtained after 60 minutes were not included.

RESULTS

The results of this study conclusively demonstrate that pressor drugs can prevent to a large degree the fall in blood pressure commonly experienced during spinal anesthesia. Figure 1 reveals that pressor drugs not only decrease the percentage of patients exhibiting a fall in blood pressure but also reduce the average blood pressure fall. For example, 457 patients or 91.4 per cent of the 500 control cases experienced a fall in blood pressure of 5 per cent or more, while only 244 patients or 48.8 per cent of the 500 cases receiving methedrine showed such a decrease. Similarly, the corresponding data for the other drugs studied were: paredrine 377 or 75.4 per cent; ephedrine 362 or 72.4 per cent; and pitressin-ephedrine 252 or 50.4 per cent. Furthermore, as Figure 1 shows, the average fall for the methedrine group was only 2.98 per cent while the control group fell on the average 36.0 per cent below the preoperation level. Likewise, the other drugs minimize the expected fall in blood pressure as shown by the average blood pressure falls of 5.3 per cent for pitressin-ephedrine, 14.5 per cent for ephedrine, and 18.6 per cent for paredrine. In each case these improvements over the control average are real and not due to chance as shown by the t values of Table III. All the drugs differ significantly from each other in their relative ability to minimize the fall in blood pressure, except that pitressin-ephedrine and methedrine were about equally effective and did not differ significantly from each other in this respect.

A further comparison of the groups was made by classifying the cases in each group

TABLE III.—*t* VALUES

Tests of significance for the relative effectiveness of various pressor drugs in counteracting the expected fall in blood pressure.

	$\bar{X}$	Con. −36.0	Par. −18.6	Eph. −14.5	P.-E. −5.3
Met.	−2.98	22.46**	10.21**	7.37**	1.41
P.-E.	−5.3	14.5**	8.65**	6.05**	
Eph.	−14.5	16.08**	3.00**		
Par.	−18.6	12.6**			

Con., Control; Par., paredrine; Eph., ephedrine; P.-E., pitressin-ephedrine; Met., methedrine; $\bar{X}$, mean. The *t* values (test for significance) for each pair of means is given in the block at the intersection of the row and column of the means being compared. The designation ** indicates the difference in means is highly significant; * indicates a significant difference. A value of *t* less than 1.96 in this table indicates the differences are not significant.

on the basis of a fall in blood pressure of 25 per cent or more from the control level. This criterion was arbitrarily selected as a decrease in pressure which might be regarded as representing a potential danger sign. The number (and per cent) of cases having a fall in blood pressure of 25 per cent or more was, respectively, for the controls 325 or 65.0 per cent; paredrine 188 or 37.8 per cent; ephedrine 148 or 29.6 per cent; pitressin-ephedrine 95 or 19.0 per cent; methedrine 98 or 19.6 per cent. Figure 2 presents this data in chart form. It is evident that there was a progressive decrease in the number and percentage of cases experiencing the designated drop in blood pressure with the use of paredrine, ephedrine, pitressin-ephedrine, and methedrine. Here again the latter two were most effective and not significantly different from each other; all other differences between drugs and between each drug and control were significant as shown by chi-square test (Table IV).

It is thus apparent that without the use of a pressor drug one can expect some degree of

TABLE IV.—CHI-SQUARE VALUES

Tests of significance of the relative effectiveness of various pressor drugs in preventing falls in blood pressure of 25 per cent or more.

	Con.	Par.	Eph.	P.-E.
Met.	210**	39.4**	13.6**	0.05
P.-E.	210**	42.6**	15.2**	
Eph.	150**	7.2**		
Par.	70.7**			

Con., control; Par., paredrine; Eph., ephedrine; P.-E., pitressin-ephedrine; Met., methedrine.
The designation ** indicates high significance.

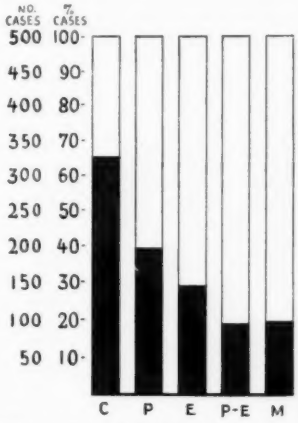

Fig. 2. The comparative effectiveness of vasopressor drugs in reducing the number (and per cent) of cases exhibiting a fall in blood pressure of 25 per cent or more. Each bar represents 500 cases (100%) for each drug and the control; the solid black portion indicates the number and per cent of cases having a fall in blood pressure of 25 per cent or more; the open bar indicates the balance of cases, i.e., those not exhibiting this degree of fall in blood pressure. *C*, Control; *P*, paredrine; *E*, ephedrine; *P-E*, pitressin-ephedrine; *M*, methedrine.

hypotension in the majority of patients given spinal anesthesia. It is also evident that some pressor drugs are more effective than others in combatting this tendency toward a lowered blood pressure. To clarify some of the factors involved in the depression of blood pressure following spinal anesthesia and to indicate the extent to which pressor drugs are of value, the data were analyzed further.

1. Level of spinal anesthesia. As would be expected there is an increased tendency for the blood pressure to fall as the level of anesthesia becomes higher. This is shown by Figure 3 where the type of operation is disregarded and the anesthesia levels are grouped as sacral, lumbar, dorsal 9-12, dorsal 5-8, dorsal 1-4, and cervical. For example, in the control cases, if type of operation is disregarded the mean percentage drop at the sacral level was 15 per cent, while at the cervical level of anesthesia it was 40 per cent.

The progressive decrease in drop of blood pressure when pressor drugs of increasing effectiveness are used is apparent from the decreased lengths of the bars at corresponding anesthesia levels. It will be noted that the

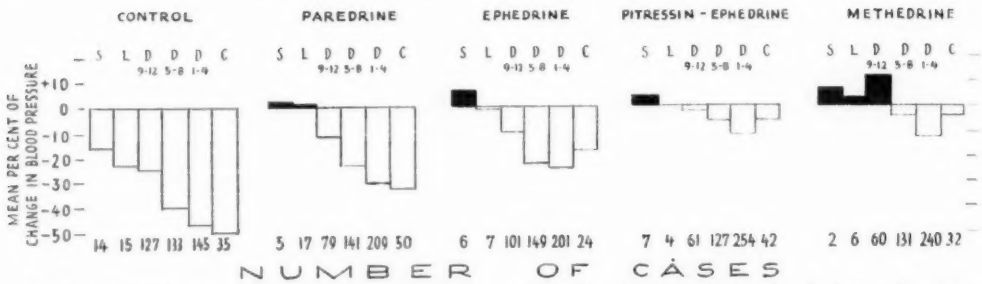

Fig. 3. The mean per cent fall in blood pressure at various levels of anesthesia, i.e., sacral, *S;* lumbar, *L;* dorsal 9-12 (*D 9-12*); dorsal 5-8 (*D 5-8*); dorsal 1-4 (*D 1-4*); and cervical, C, is given for the control and each pressor drug group. The total number of cases in each group is also given. Note the increased percentage fall in blood pressure at higher levels of anesthesia; also the lessened tendency for the blood pressure to fall when pressor drugs are used. This is particularly striking at the higher levels of anesthesia when the more effective pressors are used, e.g., pitressin-ephedrine and methedrine. Cases in which the level of anesthesia was not determined are not included.

most effective drugs, i.e., pitressin-ephedrine and methedrine exert a relatively greater effect in maintaining blood pressure in those instances where the tendency for fall is greatest, that is, at the higher levels of anesthesia. In other words, the progressively greater fall in blood pressure at higher levels of anesthesia is less apparent when methedrine or pitressin-ephedrine is used than when no pressor drug or when paredrine or ephedrine is used.

As a further comparison, a statistical analysis was made of the percentage of cases showing a fall in blood pressure of 25 per cent or more at various levels of anesthesia, with various pressor drugs. For this purpose the anesthesia levels were grouped as follows: Dorsal 10 or below, dorsal 9-5, above dorsal 5. These data are presented in chart form in Figure 4. The use of pressor drugs in all cases resulted in a highly significant improvement over the control group. Also, the results of the chi-square test given in Table V show that the differences among drugs are significant except in the cases of methedrine as compared to pitressin-ephedrine, paredrine as compared to ephedrine at levels dorsal 9-5 and dorsal 10 and below, and pitressin-ephedrine as compared to ephedrine and to paredrine at the level of dorsal 10 and below. As in previous comparisons methedrine and pitressin-ephedrine were the most effective drugs.

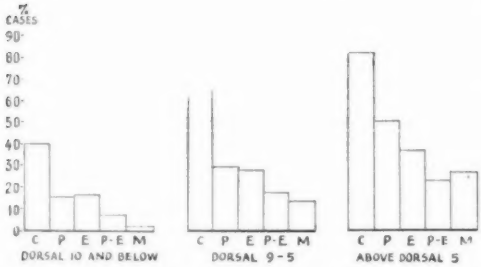

Fig. 4. Per cent of cases showing a fall in blood pressure of 25 per cent or more at different levels of anesthesia and with various pressor drugs and with no pressor drug (control). Percentage of cases having a fall in blood pressure of 25 per cent or more increases as the level of anesthesia rises; it also increases when less effective pressor drugs, or no pressor drug, are used. All differences between drugs at given levels of anesthesia are significant except for the following: Methedrine as compared to pitressin-ephedrine at all levels, pitressin-ephedrine as compared to ephedrine and to paredrine at the level of tenth dorsal and below, and paredrine as compared to ephedrine at levels dorsal ninth to fifth and tenth dorsal and below. *C*, Control; *P*, paredrine; *E*, ephedrine; *P-E*, pitressin-ephedrine; M, methedrine.

These data offer statistical support to the clinical experience that the higher levels of anesthesia are more often associated with a decrease in blood pressure. They also indicate the value of pressor agents under such circumstances.

2. Type of spinal anesthetic drug. The cases were grouped according to the spinal anesthetic drug used, for each pressor drug, and for the controls. The comparison was made on the basis of the percentage of cases in each group exhibiting a fall in blood pressure of 25 per cent or more from the initial preoperative level. These results are presented in Figure 5. Nupercaine was used in virtually all renal operations and in relatively few pa-

TABLE V.—CHI-SQUARE VALUES

Tests of significance of the relative effectiveness of various pressor drugs in preventing falls in blood pressure of 25 per cent or more at various levels of anesthesia.

Level of Anesthesia—Above D_5

	Con.	Par.	Eph.	P.-E.
Met.	139**	30**	4.09*	2.6
P.-E.	174**	49**	13.7**	
Eph.	90**	9.1**		
Par.	49**			

Level of Anesthesia—$D_{9\text{-}5}$

	Con.	Par.	Eph.	P.-E.
Met.	8.3**	11.9**	10.3**	2.4
P.-E.	69.9**	6.1**	5.5*	
Eph.	44.6**	0.06		
Par.	38.9**			

Level of Anesthesia—D_{10} and below

	Con.	Par.	Eph.	P.-E.
Met.	30**	7.3**	7.7**	1.9
P.-E.	21**	2.26	2.7	
Eph.	13.9**	0.02		
Par.	14.7**			

Con., control; Par., paredrine; Eph., ephedrine; P.-E., pitressin-ephedrine; Met., methedrine. The designation * indicates significance, while ** indicates high significance.

tients having other types of operation. Hence, nupercaine cannot be compared fairly with the other anesthetic drugs. The somewhat higher percentage of nupercaine cases having a substantial fall in blood pressure may be correlated with the higher incidence of blood pressure fall with operations at higher levels of anesthesia, such as renal and upper abdominal operations.

There appears to be no significant difference between pontocaine and procaine as regards incidence of a fall in blood pressure of 25 per cent or more when compared by the pressor drugs used; the respective percentages for the two anesthetic drugs are virtually identical with methedrine (17.1%, 17.7%), with pitressin-ephedrine (17.8%; 17.9%) and with the controls (63.2%; 34.4%) and with paredrine (33.4%; 42.3%) appear to be due to the inclusion of a larger proportion of cases with operations of the renal or upper abdominal type in the procaine group; this is shown by comparison of the anesthetic drugs with each type of operation. For example, with paredrine the respective percentages for pontocaine and procaine were: inguinal and perineal, 17.1 per cent, 17.9 per cent; lower extremity, 40 per cent, 35 per cent, lower abdominal, 42.4 per cent, 38.4 per cent; upper abdominal, 66.6 per cent, 62.4 per cent—none of these differences is significant. Similarly with ephedrine the respective values were: inguinal and perineal, 15 per cent, 8.7 per cent; lower extremity, 21 per cent, 36 per cent; lower abdominal, 27 per cent, 43.6 per cent; upper abdominal, 55 per cent, 39.7 per cent; when tested by the chi-square method none of these differences was significant except in the case of the lower abdominal group.

3. Initial blood pressure. The effect of the initial preoperative blood pressure level on the subsequent fall in blood pressure was analyzed by determining the percentage of cases at various initial blood pressure levels which experienced a fall in blood pressure of 25 per cent or more. The results are presented in Figure 6. It will be seen that with higher initial blood pressure levels the percentage of cases having a marked fall in blood pressure increases. It is also to be noted that at each initial blood pressure level the effectiveness of pressor drugs is demonstrated, the relative effectiveness of the various pressor agents being the same as noted by other bases of comparison; i.e., methedrine and pitressin-ephedrine were most effective.

4. Age of patient. In order to determine the effect of age, the number of cases in each age group, which had a fall in blood pressure of

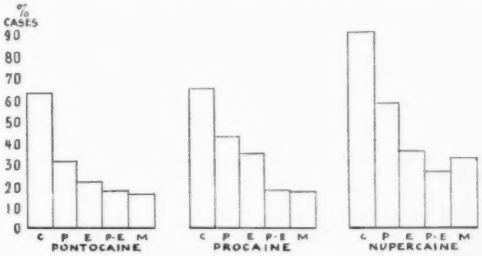

Fig. 5. Per cent of cases showing a fall in blood pressure of 25 per cent or more for each pressor drug grouped according to anesthetic agent used. The cases receiving nupercaine were mostly renal operations, hence, this group is not comparable to the other groups. The results with pontocaine and procaine do not appear to be significantly different.

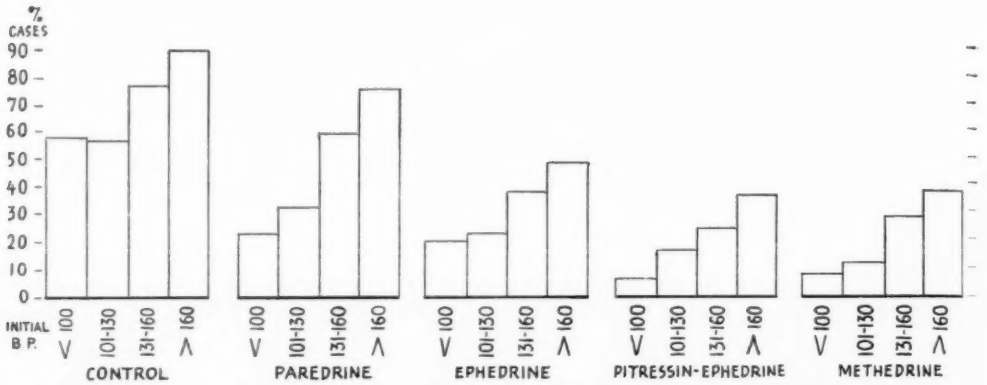

Fig. 6. Per cent of cases with various initial preoperative blood pressure levels having a fall in blood pressure of 25 per cent or more, grouped by pressor drugs used and controls. Subdivisions have been made according to 4 arbitrarily selected levels of systolic pressure, i.e. less than 100 millimeters mercury, 101 to 130 millimeters mercury, 130 to 160 and over 160 millimeters mercury. Note the increased percentage of cases with at least a 25 per cent fall in blood pressure as the initial blood pressure level increases, and with the less effective pressor drugs and with no pressor drug.

25 per cent or more were compared with the total number of cases in each group. Figure 7 shows not only the distribution of total cases among the various age groups, but also the number of cases in each group having a marked (25% or more) fall in blood pressure; in general the percentage of the latter increases with age. This is probably correlated to some extent with the tendency for the initial blood pressure to be higher with increased age.

It will be seen that the pressor drugs were effective at all ages and especially so with the younger age groups. It was a rare occurrence for patients below 20 years of age to experience a dangerous fall in blood pressure after receiving methedrine, pitressin-ephedrine, or ephedrine. With increasing age the number and percentage of patients in the danger zone tended to increase for all five drug groups. It will also be seen that pitressin-ephedrine and methedrine were more effective than ephedrine alone or paredrine.

DISCUSSION

One of the objections to the use of spinal anesthesia has been the decrease in blood pressure so frequently seen following its administration. The extent of this problem is evident when we review the data obtained from the 500 cases in the control group who received no pressor drug. This group represents a cross section of the types of surgery normally managed under spinal anesthesia and includes such major procedures in the upper abdomen as gastrectomy, choledochostomy, splenectomy, nephrectomy, as well as surgical procedures lower in the abdominal cavity, operations on the extremities, and the perineum. Obviously the percentage of patients showing a decrease in blood pressure would be greater if there were more upper abdominal surgery, but since all of the groups are about equal in this regard it is interesting to note that when no pressor drug was used, blood pressure fell an average of 36 per cent from preoperative level. Of the 500 patients 325 (65%) showed a decrease in systolic pressure of 25 per cent or more.

The pathological physiology underlying the decrease in arterial pressure had been studied by many investigators and, although there is not complete agreement, it is evident that a variety of factors are involved in the production of this hypotension. The major circulatory alterations caused by spinal anesthesia will be briefly reviewed. One form is the paralysis of vasoconstrictor (sympathetic) fibers to arterioles. This leads to arteriolar dilatation and a reduction in peripheral resistance. Since these fibers arise from the spinal cord in the thoracolumbar area, the

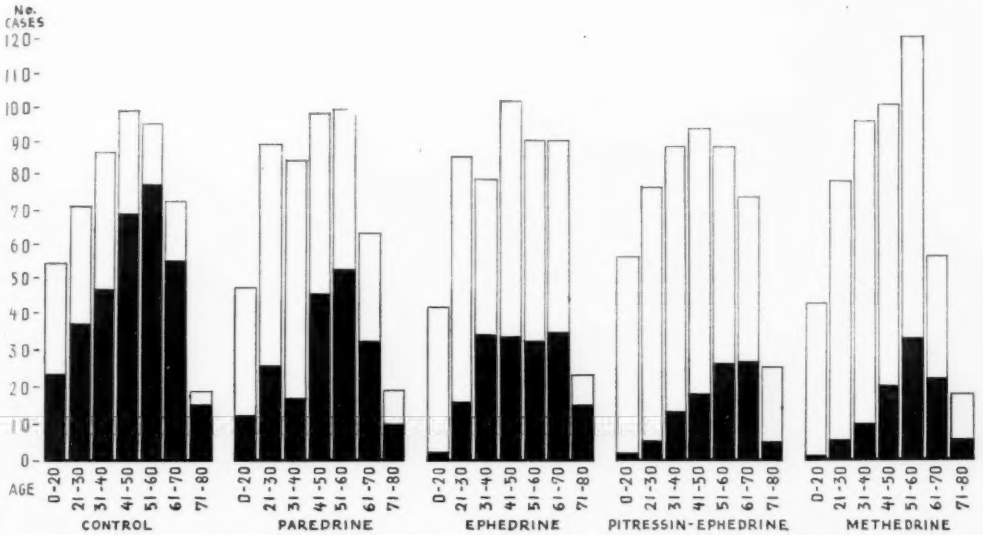

Fig. 7. Total number of cases at various age levels, for each pressor drug and for the controls, are shown by the open bars. The solid black bars indicate number of cases in respective age groups which experienced a fall in blood pressure of 25 per cent or more. In general the percentage of cases with fall in blood pressure increases with age.

higher the level of anesthesia, the more pathways are blocked. Smith and his co-workers (1939) have questioned the importance of central constrictor impulses in the maintenance of arteriolar tone, but it is difficult to avoid the conclusion that such impulses do play a part.

Spinal anesthesia also affects the venous circulation. Paralysis of skeletal muscles in the legs abolishes the pump action of these muscles and reduces venous return to the right heart. Varying degrees of intercostal muscle paralysis likewise decrease the respiratory thoracic pump action bringing blood into the great veins. Furthermore, there is, in all probability, actual dilatation of peripheral veins and venules with pooling of blood just beyond the capillaries. All of these factors decrease venous return, venous pressure falls, and cardiac output is reduced. These facts have been substantiated experimentally (Burch and Harrison, 1930; Adriani and Rovenstine, 1940).

Finally, paresis or paralysis of intercostal muscles decreases respiratory minute volume and tidal exchange (Stevens and Waters, 1932). The resulting anoxia damages cell function throughout the body, particularly in the central nervous system, and mechanisms which might compensate for some of the alterations in function become weakened and less effective.

A pressor drug is therefore useful for a number of reasons. Such a substance can (a) produce vasoconstriction peripherally by a direct action on arteriolar muscle, (b) increase cardiac output by direct stimulation of the myocardium, (c) stimulate the vasomotor center, and (d) constrict veins and venules. All of these actions would be helpful in preventing the circulatory changes described. The exact combination of pharmacological effects appears to differ with different sympathomimetic substances. Thus, Starr and coworkers (1937) have shown ephedrine to produce a rise in systolic pressure in normal individuals largely as the result of an increased cardiac output secondary to cardiac stimulation. Peripheral resistance may even be decreased under such circumstances. Fassett (1945) on the other hand finds that methedrine does not increase cardiac output in normal subjects, but raises peripheral venous pressure and increases total peripheral resist-

ance greatly. Iglauer and Altschule (1940) report that paredrine has the property of constricting veins by a direct peripheral action. Finally, pitressin owes its pressor activity to a constrictor action on capillaries and arterioles. This action is a direct one on the vascular musculature and is not related to adrenergic vasomotor nerves (11).

The facts here outlined were obtained from studies on normal subjects. That such data may not apply under conditions of spinal anesthesia is suggested by observations of Courmand, Bloomfield, and Lawson (1945) that patients with low blood pressure as the result of acute alcoholism showed marked increases in cardiac output following the intravenous administration of methedrine, a drug which in normal man does not produce this effect. It is evident, therefore, that the basic circulatory actions of pressor drugs used in this series are well documented but that each substance presents a specific combination of these actions, a combination which may vary according to the experimental conditions.

On the basis of data obtained from our 2500 cases, certain conclusions can be reached. First, without pressor drugs spinal anesthesia can be expected to produce a decrease in blood pressure in a high proportion of cases. Second, this decrease in blood pressure is more likely to occur with higher levels of anesthesia, in the older age groups and in patients whose initial level of arterial tension is above normal. Third, the drop in blood pressure is not related to the type of anesthetic agent used, at least as far as procaine and pontocaine are concerned. Fourth, almost any pressor drug is useful in lessening the incidence and degree of this spinal anesthesia hypotension. Fifth, certain drugs are more effective in this regard than others. In this series the combination of pitressin-ephedrine and methedrine alone were more effective than ephedrine alone or paredrine. In the 500 patients receiving methedrine, the average fall in blood pressure was 3 per cent in contrast to 5.3 per cent for pitressin-ephedrine, 14.5 per cent for ephedrine alone and 18.6 per cent for paredrine. These differences are statistically significant except for the differences between methedrine and pitressin-ephedrine.

Having two pressor combinations which have proved equally effective in maintaining circulatory adequacy during spinal anesthesia, how can one choose between the two? This decision rests largely on the side actions caused by the drugs, and the body of evidence in this regard is against the use of pitressin-ephedrine.

Objections to the combination of pitressin and ephedrine include the following points: (1) Pitressin stimulates smooth muscle of the intestinal tract and not infrequently in our experience caused severe abdominal crampy pains. The duration of this discomfort rarely exceeded 15 minutes. (2) There was a higher incidence of nausea and emesis in the patients receiving pitressin-ephedrine than in any of the other groups. Whether this is related to the intestinal action just discussed is uncertain. (3) The striking facial pallor following pitressin constitutes a psychic disadvantage, since the grey-green color, although unaccompanied by any subjective recognition of this appearance, suggests a serious vascular condition to uninformed observers. The peculiar color is due to marked constriction of vessels in the "blush area." (4) Excessive rises in blood pressure were occasionally seen. Systolic levels well over 200 millimeters of mercury in normal patients were observed to last for several hours. These reactions usually were accompanied by severe headache. (5) Although we did not note any uterine cramps, this complication has been reported (Kirklin and Seedorf, 1939). Such a reaction is more common early in the menstrual month. (6) A final objection is the action of pitressin in constricting coronary arteries. Although the addition of ephedrine is alleged to minimize such a response, the possibilities of such an untoward reaction must be considered from the theoretical standpoint.

For these reasons we conclude that methedrine is a superior pressor agent. The only unpleasant side action of the substance which we noted was the occurrence of prolonged stimulation of the central nervous system, taking the form of talkativeness and insomnia. This was not marked in the surgical patient but was readily apparent when the drug was administered to volunteer subjects.

It should be pointed out that all of the data discussed in this paper are based on the particular doses of the drugs used in the series. Had other doses been employed the results might have been different. Thus, some workers employ 75 to 100 milligrams of ephedrine sulfate prior to spinal anesthesia. Others use two doses of pitressin. With these larger amounts there undoubtedly would have been fewer patients exhibiting decreases in blood pressure. Our doses were, however, those in standard use in many clinics. In all probability one should adjust the dose of a pressor drug according to the expected level of spinal anesthesia, the age of the patient, and the initial level of blood pressure. Thus, for example, smaller doses are indicated for such operative procedures as hemorrhoidectomy, where anesthesia of sacral roots suffice; smaller doses can also be used in younger individuals and in those with normal blood pressure. If a routine dose is adopted, however, our data indicate that 20 milligrams of methedrine intramuscularly will be more effective than will any of the other drugs used in this investigation.

This study supports the work of Prescott (1944) and Hudson and Paradis (1945) indicating that methedrine is a valuable sympathomimetic anine as far as raising a lowered blood pressure is concerned. Prescott compared the pressor activity of methedrine, paredrine, neosynephrine, and paredrinol in surgical patients with systolic blood pressure of 80 millimeters or less. Criteria used included rise of systolic and pulse pressure, speed and duration of action, and relative freedom from side effects. On the basis of the results obtained the clinical effectiveness of the four pressor drugs examined was in the order listed, i.e. methedrine, paredrine, neosynephrine, and paredrinol.

The time of administration of the drug should be judged so as to afford a maximum pressor effect when circulatory depression from spinal anesthesia is at its peak. Thus, one must know how long such a drug takes to act when given intramuscularly, what the duration of action is, and when one can anticipate the greatest decrease in blood pressure following the anesthetic. The onset of action of methedrine when administered intramuscularly is within 3 to 4 minutes (i.e., rise of 10 mm. Hg. systolic), reaching a maximum at an average of 17 minutes (4 to 38 minutes—Prescott, 1944). The duration of action of this drug averages 2 hours (Dodd and Prescott, 1943). Since the typical hypotension following spinal anesthesia occurs within the first 20 minutes, it is our opinion that methedrine can be injected into the deep muscles of the back at the time of the lumbar puncture. In our experience such a technique has proved quite satisfactory. If one is particularly concerned about the prevention of hypotension, i.e., in arteriosclerotic, hypertensive cardiovascular disease, in patients with a history of cerebral or coronary thrombosis, a somewhat longer time interval should be allowed to elapse for the injection of the pressor drug to the introduction of the anesthetic into the subarachnoid space. Since the rise in blood pressure following the intramuscular administration of most pressor drugs is rarely over 30 millimeters of mercury systolic, we are not concerned with the adverse effects of these substances in cardiac patients, but feel convinced, on the other hand, that their use is definitely indicated prophylactically in such patients (Dripps, 1944). It is in these patients that a decrease in blood pressure is far more hazardous than a slight rise.

SUMMARY

The vascular response of 2500 patients receiving spinal anesthesia has been studied. Five hundred patients received no pressor drug prior to anesthesia and the average fall in systolic blood pressure in this group was 36 per cent from the preoperative level. Five hundred patients received paredrine in an attempt to maintain blood pressure. The average fall in this group was 18.6 per cent. Five hundred patients given ephedrine showed an average decrease of 14.5 per cent. Five hundred patients receiving methedrine showed a 3.0 per cent decrease in systolic blood pressure. Methedrine and pitressin-ephedrine were therefore most effective.

Methedrine is preferred to the combination of pitressin-ephedrine for a variety of reasons. The former drug is administered intramuscu-

larly in doses of 20 milligrams at the time of lumbar puncture. Onset of action is prompt and duration is prolonged.

The incidence and degree of the decrease in blood pressure which follows spinal anesthesia is greater with higher levels of anesthesia, in older individuals and in patients with initial blood pressures which are above normal. There is no difference in vascular response when procaine and pontocaine are used as spinal anesthetic agents.

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THE USE OF TYROTHRICIN IN SURGICAL INFECTIONS

DONALD D. KOZOLL, M.D., KARL A. MEYER, M.D., F.A.C.S., WILLIAM S. HOFFMAN, Ph.D., M.D., and SEYMOUR LEVINE, M.A., Chicago, Illinois

THE peculiarities of a surgical infection are such that they frequently respond best to agents applied directly to the site of infection. With the new therapeutic era opened by the antibiotics, interest in the development of locally applied antibiotics was only natural. Among the first of these to be discovered was gramicidin, described by Dubos in 1939. It was found to be lethal to gram positive cocci (7, 8, 10, 11, 13, 16, 22) and effective in the treatment of a large variety of streptococcal lesions of the skin, sinuses, pleura, and bone (9, 12). The material was not destructive in its effect on tissues except for a pronounced hemolytic effect upon erythrocytes; removal of the hemolytic factor resulted in a loss of its bacteriocidal powers (14). In its antibacterial behavior it acted like an anionic detergent (15). In comparison with another closely related antibiotic, tyrocidin, gramicidin was found to be less stable, slightly more cytotoxic, and highly insoluble; tyrocidin could keep gramicidin in suspension and had more of an inhibiting effect on certain gram negative flora.

It was later found that the crude material which contained both gramicidin and tyrocidin could combine the bacterial potency of the former with the stability and solubility of the latter. The crude material—tyrothricin—represents the form in which these antibiotics are now being applied. Preliminary reports have indicated a wide field of usefulness of this drug (5, 9, 19, 22) but in the enthusiasm for the use of penicillin, few controlled clinical studies have been undertaken to evaluate this antibiotic, in spite of the fact that it offered certain theoretical advantages over penicillin. In the first place, tyrothricin has been found to have a more rapid lethal effect upon sensitive organisms. Second, because of low absorption and penetration through tissues, a higher local concentration could be attained. A decreased excretion would also enhance the local concentration, a greater stability ensures prolonged action, and because of the high dilutions at which tyrothricin is still effective, it becomes clinically an inexpensive antibiotic.

The following study was outlined to investigate a specific tyrothricin preparation made available to use for this purpose:

1. To observe the clinical effectiveness of tyrothricin in the treatment of a variety of surgical lesions as judged by changes in the exudate, area of the wound, granulation, and pain.

2. To observe the effect of tyrothricin upon normal and inflamed tissues.

3. To observe signs of local and systemic toxicity.

4. To study the effect of tyrothricin upon the bacteriological flora of the wound.

5. To observe evidences of hemolysis by following the changes in the hematocrit, hemoglobin, and icteric index.

6. To compare tyrothricin with other methods of treatment.

METHOD OF STUDY

The project was undertaken by a team consisting of two nurses, a bacteriologist, a hematological technician, a photographer, and a surgeon. The same nurses dressed the wounds to standardize the method of dressings, the obtaining of cultures, and the preparation of the solutions. The same bacteriologist carried out the bacteriological studies throughout the period of the study. The surgeon selected all cases for treatment and determined the clinical result.

The tyrothricin used in this study was furnished to us as a 2.5 per cent alcoholic solution in a sterile ampul containing 20 cubic

From the Departments of Surgery of the Cook County Hospital, Northwestern University Medical School and Cook County Graduate School, from the Hektoen Institute for Medical Research of the Cook County Hospital, and from the Department of Bacteriology, University of Illinois.

Dr. Kozoll, Abbott Fellow, Department of Surgery, Northwestern University Medical School. An abridgment of a thesis submitted by Dr. Kozoll to the Graduate School of Northwestern University for the degree of Master of Science in Surgery.

centimeters of the material. This was added to a liter flask of sterile distilled water, thus making a solution that contained approximately ½ milligram of tyrothricin per cubic centimeter of solution. Toward the end of the study in a few cases, a more concentrated preparation was used (1 mgm. per c.c.) or 40 cubic centimeters of the 2.5 per cent solution diluted to a liter. This was done for comparative purposes to note the effect of the stronger solution on the speed of healing. All solutions were made up freshly each day and any unused solution was discarded at the end of the day.

At the beginning of tyrothricin therapy, all wounds were photographed. The photographs were identified in the same manner as roentgen-ray films and a metric scale on the marker provided a means of permanently recording the size of the wound, which we found correlated well with actual measurements of the wound, for the differences recorded far exceeded the possible error. Special mimeographed sheets provided columns for entries of pertinent details of the clinical history and permitted daily entry of data concerning the treatment, changes in the wound, the quantity of the drug used, temperature, pulse, respiration, and all the laboratory data. The photographs were retaken at weekly or biweekly intervals as indicated. Cultures and venous blood for hematological study were also taken before the start of the therapy.

Tyrothricin was used in the form of a wet gauze dressing. The quantity of solution necessary to saturate the gauze was measured in a sterile graduate before application. The moist gauze was then packed loosely into the wound, an absorbent placed over the gauze, followed by a layer of cellophane, parchment, or wax paper to control evaporation or loss of tyrothricin solution. Dressings were held in place by gauze rolls, adhesive, binders, or splints as the lesion required. Dressings were changed daily by the same personnel.

The bacteriological procedure was carried out as follows. The nurse dressing the wound was carefully instructed to remove the same amount of exudate from approximately the same area of the wound so that the bacteriological counts might be standardized as much as possible. At first the cultures were taken daily, but we soon learned that cultures taken every 2 or 3 days were frequent enough. The exudate was recovered by a dry sterile swab which was immediately placed into a test tube containing 2 cubic centimeters of sterile distilled water to help keep the cultures moist. All swabs reached the bacteriologist within 2 hours from the time they were taken from the wound. The bacteriologist agitated the swab in the water to displace as many of the bacteria as possible, and then the swab was placed in a tube of brain broth. The brain broth was incubated at 37 degrees C. for 24 hours after which a gram stain was made and examined microscopically. One tenth cubic centimeter of the distilled water containing the organisms was inoculated deeply into melted agar containing 0.2 cubic centimeter of blood, and poured into a sterile plate. The plate was incubated for 48 hours aerobically at 37 degrees C. after which time the colonies were counted. When it was anticipated that the infection was extremely heavy, appropriate dilutions of the original samples were made in distilled water. A special effort was made to differentiate streptococci, staphylococci, diphtheroids, and gram negative bacilli, particularly Pseudomonas pyocyaneous. A 4 millimeter loopful of the specimen was streaked on a blood agar plate and incubated aerobically at 37 degrees C. for 48 hours. At the end of this time well isolated colonies of varying morphology were transferred to blood agar slants and identified (2). At first a second plate was streaked and incubated anaerobically in a platinum catalyst type anaerobic jar, illuminating gas being used instead of hydrogen gas. It was soon found that so few of the wounds possessed an anaerobic flora, that it was unnecessary to use anaerobic technique routinely. Instead, the brain broth culture, described in the foregoing, was examined and when any suspiciously appearing gram positive rods were found, an anaerobic streak plate was prepared from the brain broth. Anaerobes were identified by the use of the technique described by Reed and Orr.

Hematological studies were carried out on venous blood drawn before the start of the therapy and at weekly intervals thereafter.

Heparin was used as the anticoagulant for plasma. Determinations included the sedimentation rate, hematocrit, hemoglobin, total serum protein, and icteric index. The sedimentation rate was performed by the Wintrobe method, correction being made for abnormally low hematocrits. Hemoglobin determinations were made on heparinized venous blood, the photoelectric method being used. Total serum proteins were studied by the specific gravity method of Barbour-Hamilton. Icteric indices were carried out on serum in the usual manner.

MATERIAL

The clinical material studied is listed in Table I. It consists of 77 cases of surgical infections of a wide variety such as is encountered in the charity wards of a general hospital. No deliberate attempt was made to select cases, but certain fundamental surgical principles were followed: i.e., only draining infections which communicated with the exterior were considered. At first no attention was paid to the blood supply of the part but it was soon learned that the treatment was doomed to failure in the presence of gangrene. Infected postoperative wounds were the most frequent lesions treated, of which there were 19. Infected varicose ulcers were next in frequency and constituted a group of 10 patients. There were 7 patients with cellulitis and 7 with abscesses, 5 with empyema and 5 with burns. The remainder were quite varied in nature. All patients were hospitalized for the entire period of study and received no other therapy conjointly with the tyrothricin therapy.

There were 49 white and 28 negro patients, 47 being males and 30 females. The oldest patient was 79 years and the youngest 2 years of age. There was an additional group of patients studied privately in other hospitals but these are not included for statistical appraisal because either the photographic evidence or the bacteriological studies were incomplete.

The majority of these patients were referred to us after their lesions had proved refractory to a variety of other methods of treatment, which included the use of Dakin's solution, Dakin's with saline, saline packs, sulfonamides, xeroform gauze, vaseline gauze, boric acid solution, ultraviolet light, and parenteral penicillin. These, therefore, act as control measures in evaluating the drug under investigation. Included were 6 cases with bilateral lesions in which one lesion was treated with tyrothricin and another with a control preparation. These we feel offer more crucial tests of comparison than a parallel series of patients with unilateral lesions. The variability among patients and types and degree of infections is so numerous that only a series of several hundred cases would offer statistically significant evidence.

RESULTS

A. Clinical. The criteria for clinical improvement in the treatment of the infection included the disappearance of all visible signs of infection, the decrease in the amount of exudate, the growth of viable healthy granulation tissue, the growth of epithelium over the granulation tissue, and a decrease in the size of the wound as verified by actual measurement. According to these criteria, clinical results were placed in three categories: excellent, fair, and poor.

Table I lists the various infections treated with the results evaluated as indicated above. Of 77 cases treated, 50 (65 per cent) showed excellent results, 8 (10 per cent) showed fair results, and 19 (25 per cent) showed poor results. It will be noted that 18 out of 19 cases of postoperative wound infection responded with excellent results and one gave a poor result. In the 10 cases of infected varicose ulcers, there were 7 excellent results with tyrothricin treatment, 1 was fair and 2 were poor. All of 7 cases with cellulitis responded excellently, whereas of the 7 cases of abscesses, 5 showed an excellent result and 2 poor, the latter were ischiorectal abscesses in debilitated patients. Four of the 5 patients with empyema and open drainage responded well to tyrothricin. In 1 case of an abscess due to Friedlaender's bacillus infection, the result was only fair. Of 5 infected burns treated, the result was excellent in 1, fair in another, and poor in 3. All 3 cases of decubitus ulcers responded excellently. Two of three lacerations

TABLE I.—CLINICAL RESULTS IN 77 PATIENTS WITH SURGICAL INFECTIONS TREATED WITH TYROTHRICIN

Lesion	No. of Cases	Excellent result	Fair result	Poor result
Postoperative wound	19	18		1
Varicose ulcer	10	7	1	2 (1-rash)
Cellulitis	7	7		
Abscess	7	5		2
Empyema	5	4	1	
Burn	5	1	1	3
Laceration	3	2		1
Osteomyelitis	3			3
Decubitus ulcer	3	3		
Carcinomatous ulcer	2		1	1
Carbuncle	2		2	
Luetic ulcer	2	1		1
Infected dermatitis	2	1	1	
Infected amputation stump	2	1	1	
Buerger's disease	1			1
Infected fracture	1			1
X-ray burn	1			1
Tenosynovitis	1			1
Fistulae (perinephric)	1			1
Totals	77	50 (65%)	8 (10%)	19 (25%)

TABLE II.—DURATION OF TREATMENT WITH TYROTHRICIN OF 77 PATIENTS WITH SURGICAL INFECTIONS

Length of treatment	Clinical result		
	Excellent	Fair	Poor
Weeks 1	4		7
2	11	2	4
3	6	2	5
4	16	3	2
5	7		1
6	1		
7	1	1	
8	4		
Total	50	8	19

responded well whereas the third did not. Of 2 secondarily infected luetic ulcers which had not responded to antiluetic therapy alone, 1 showed an excellent result with tyrothricin, and the other a poor one. The patients with carbuncles responded only fairly. Three patients with osteomyelitis (diabetics) and 1 patient each with an infected fracture, an x-ray burn, a carcinomatous ulcer, tenosynovitis, and a perinephric fistula, all did not improve with tyrothricin therapy.

Table II presents the length of treatment required in each of the groups classified as to result. It is to be noted that of the patients with excellent result, 4 responded within 1 week of treatment, 11 within 2 weeks, 6 within 3 weeks, and 16 within 4 weeks of treatment. In other words 37 out of 77 patients responded to tyrothricin with excellent results within 1 month; 13 others required an additional month. The group with fair results is too small for statistical evaluation. The short time of treatment in the group with poor results was due to the fact that in many of these cases either death or some complication supervened which required discontinuance of treatment.

The speed of healing was usually proportionate to the initial size of the wound. The general clinical impression was gained that tyrothricin solution directly or indirectly speeded the formation of granulation tissue. Epithelization was also promoted so that skin grafting was necessary in only 5 of the 50 cases showing excellent results. Even the decision to do skin grafting was motivated by a desire to shorten the period of hospitalization. By indirect measurement of all wounds as recorded on photographs (instead of direct measurements of the wounds themselves) the percentage decrease in the area of the wound varied from 36 per cent to 100 per cent in the cases showing excellent results, with an average of 70.7 per cent. The number of cases in the group with fair results do not permit statistical evaluation, but the clinical impression was that there was appreciably less healing. In the group with poor results there was little decrease in the size of the wound, and in some cases the wound increased in size.

The 6 cases with bilateral lesions in which tyrothricin was applied on only one lesion merit detailed analysis. The first of this group was that of a severe pyocyaneous infection of both hands following third degree burns. The

TABLE III.—TYPE OF SURGICAL INFECTIONS TREATED IN THIS STUDY AND BACTERIAL FLORA SEEN WITH EACH LESION*

Lesion	No. of cases	Staph. albus	Staph. aureus	B. hem. strep.	Nonhem. strep.	Pyocyaneus	Diphtheroids	Staph. citreus	Gram+ anaerobe
Postoperative wound	19	5	15	8	3	10	12		1
Varicose ulcer	10	3	10	4		6	8	1	
Abscess	7		7	4	1	5	6		
Cellulitis	7	1	7	6	1	3	7		
Empyema	5		4	4	2	4	4		
Burn	5	2	4	2		3	4		
Decubitus ulcer	3	1	3	1		2	3		
Laceration	3	2	2	1	1		1		
Osteomyelitis	3		3	1	1		3		
Luetic ulcer	2	1	2	1		2	2		
Infected dermatitis	2	1	1	1		1	1		
Infected amputation stump	2		2	1		2	2		
Carbuncle	2	1	2	1	1		1		
Carcinomatous ulcer	2		2	1		1	2		
Infected fracture	1		1	1		1	1		
X-ray burn	1		1				1		
Tenosynovitis	1	1	1	1			1		
Perinephric fistula	1	1					1		
Buerger's disease	1		1			1	1		
Total	77*	19	68	38	10	41	61	1	1

*Total number of organisms will be greater than total number of cases because each wound will vary as to the number of different organisms it contains.

right hand was treated with tyrothricin while the left was treated with equal parts of boric acid and vinegar; the tyrothricin treated hand did much more poorly and tyrothricin treatment had to be discontinued. The second case of this group was that of a patient with bilateral varicose ulcers of almost identical initial size (Fig. 8). The right ulcer, which was treated with tyrothricin, showed a much more rapid clearance of exudate, granulation, epithelization, and disappearance of pain, than did the left ulcer which was treated first with Dakin's saline solution and then saline solution alone. Also bacteriologically, the tyrothricin treated wound responded more favorably. Case 3 of this group was that of an infected epidermophytosis and edema of both legs. There was no apparent difference between the leg treated with tyrothricin and the one treated with saline, although the former was the more seriously involved. Case 4 of the group (Fig. 17) involved a patient with varicose ulcer on the right leg measuring 36.1 square centimeters and one on the left leg measuring 7.4 square centimeters. The right ulcer was treated with tyrothricin and the ulcer healed completely in 3 weeks while at the end of the same period the left ulcer, which had been treated with saline, still measured 2 square centimeters. The fifth case was one of hemiplegia and decubitus ulcers on both heels; the right ulcer, treated with tyrothricin for 4 weeks, showed an 80 per cent decrease in area and filled with granulation tissue, while the left one, treated with saline during that time, was still purulent and had not decreased in size. The remaining case of this series was another one of bilateral varicose ulcers in which the ulcer treated with tyrothricin responded about as well as the one treated with Dakin's saline solution although the former wound was by far the larger (Fig. 19).

In the few experiments in which the strength of tyrothricin solution was doubled (1 mgm. per c.c.) the speed of granulation appeared to increase. For example, if the size of the lesion

TABLE IV.—INFLUENCE OF TYROTHRICIN SOLUTION UPON INDIVIDUAL BACTERIA IN 77 TREATED CASES

Organism	Colonies disappeared	Colonies decreased	Colonies increased	Colonies appeared
Hemolytic streptococcus Group A*	18	5		
B**	1			1
C***	1	4	3	1
Nonhemolytic streptococcus Group A	2	2		1
B				
C	1	1	1	1
Staphylococcus aureus Group A	16	17	6	1
B	1	3	3	1
C	1	3	11	1
Staphylococcus albus Group A	3	6	4	
B	1			
C	1	2	2	
Pseudomonas pyocyaneus Group A	3	4	4	17
B				5
C	1		6	4
Diphtheroids Group A	4	13	10	11
B	2	2	3	
C	5	1	7	1

* Group A, treated with excellent results (50 cases)
** B, treated with fair results (8 cases)
*** C, treated with poor results (19 cases)

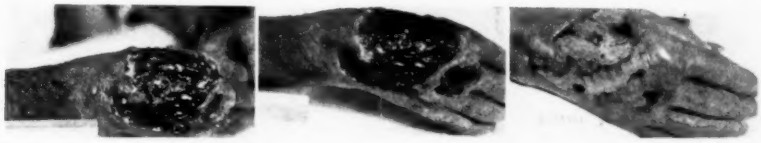
in Figures 9, 13, and 20 is compared with some of those in earlier cases (Figs. 2, 3, 7) the increased speed with which these larger lesions became granulated may be attributed to the stronger solution. Similarly, in cases in private practice where a change of tyrothricin dressing could be carried out every 4 hours, a more rapid healing and granulation was noted. Neither the increased strength of the solution nor the more frequent change of dressing produced any tendency to local or systemic reactions.

One patient not included in the series under experimental investigation is of particular interest. The patient was a 29 year old white female who had a hemolytic streptococcal (Meleney) gangrene involving the entire thickness of the abdominal wall of the right lower quadrant down to the musculature, and extending onto the right thigh and vulva. The patient had received every therapeutic adjunct available including zinc peroxide, sulfa drugs locally, orally, and intravenously, and parenteral penicillin. Within 8 days of tyrothricin therapy (applied every 4 hours night and day) all signs of necrosis and cellulitis had disappeared, the entire ulcerated area was covered with healthy granulation tissue, and the patient for the first time in several weeks did not require morphine for change of dressings and expressed the desire to get out of bed.

B. Bacteriological. The varieties of organisms encountered in each of the various types of lesions and their relative frequency is indicated in Table III. It will be noted that Staphylococcus aureus was found most frequently, then the diphtheroids, followed by Pseudomonas pyocyaneus, beta hemolytic streptococcus, Staphylococcus albus, and alpha nonhemolytic streptococcus. Though the flora in any given patient was identified with consistency, the colony counts at times show unusual variations. This was thought to be due either to an accidental difference in the quantity of exudate removed with the swab or to the pleomorphic nature of the diphtheroids which frequently took on the morphologic features of staphylococci or streptococci. For this reason, in a number of cases, though the total colony count was always estimated, the individual organisms were identified solely as being present or absent.

The detailed effect of treatment upon individual groups of organisms is presented in tabular form in Table IV. It was readily apparent that the beta hemolytic streptococcus was the most susceptible organism treated, followed by the Staphylococcus aureus, and then Staphylococcus albus. Tyrothricin appeared to have little favorable effect upon gram negative flora as the pyocyaneus and diphtheroids; in fact, these two organisms demonstrated a pronounced tendency either to proliferate or to make their initial appearance in the course of treatment.

A correlation between bacteriological and clinical results was also seen in studying the results indicated in Table IV. For, while all hemolytic streptococci either were killed or decreased in the group that gave excellent

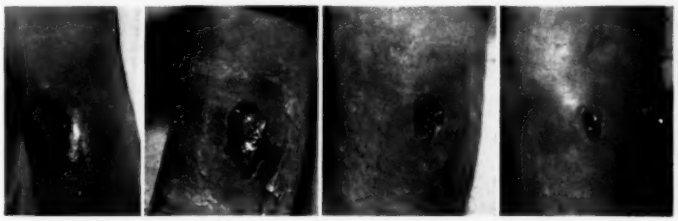


	Contro	11 days	2 weeks after skin graft
Bacteriology			
Number of colonies	200,000	32,000	
Staphylococcus albus	+	+	
Staphylococcus aureus	+	+	
Area of wound—sq. cm.	60.3	60	0
Treatment	Saline dressings	300 mgm. tyrothricin	Skin graft

Fig. 1. Infected traumatic laceration of the hand treated with tyrothricin. After 11 days of treatment there was no significant decrease in the size of the wound but such a marked clearing of all exudate and growth of granulation tissue, that a skin graft was attempted which resulted in a 90 per cent "take." A decrease in the bacteriological colony count was noted.

clinical results, the results in the group that showed poor clinical effect were also poor from the bacteriological point of view. The same correlation could be deduced from studying the responses of Staphylococcus aureus to tyrothricin.

The bacteriological findings in the patients with bilateral lesions presented findings of particular interest. In the patient with burns due to frostbite of both hands, the hand treated with tyrothricin revealed before treatment 165,120 colonies of Staphylococcus albus, pyocyaneus, and diphtheroids; after treatment, culture showed less than 100 colonies of Staphylococcus albus, but over 1,000,000 colonies of pyocyaneus (principally) and diphtheroids. The left hand which was treated as the control showed at the start 750,000 colonies of Staphylococcus aureus, pyocyaneus, and diphtheroids, and this rose to 1,008,000 with the same flora. The second case (Fig. 8) bilateral varicose ulcers, showed

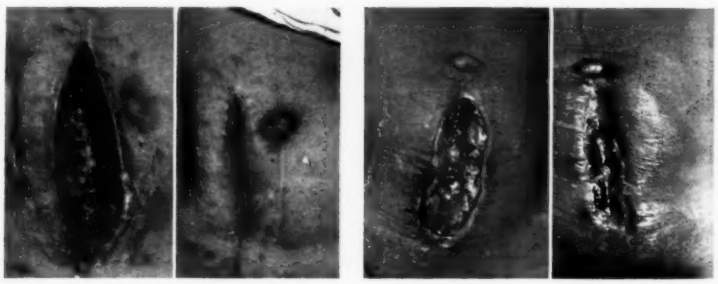


	Control	7 days	16 days	22 days
Bacteriology				
Number of colonies	100,000	100,000	37,120	1,100
Hemolytic streptococcus	+	+	+	0
Staphylococcus albus	+	+	+	+
Diphtheroids	+	0	0	0
Area of wound—sq. cm.	16	12	2.5	1.8
Treatment	Saline dressings	150 mgm. tyrothricin	310 mgm. tyrothricin	300 mgm. tyrothricin

Fig. 2. Streptococcal cellulitis of the leg with marked edema and induration. Central area around incision for drainage sloughed but within 22 days of treatment with 300 milligrams tyrothricin, the entire area had granulated and epithelized. The bacteriological cultures, which were predominantly hemolytic streptococci, showed a complete disappearance of all streptococci and diphtheroids, and a marked decrease in the number of staphylococci.

	Control	7 days	15 days	28 days
Bacteriology				
Number of colonies	200,000	128,000	20,400	40,400
Hemolytic streptococcus	+	+	+	<100
Staphylococcus aureus	+	+	+	+
Area of wound—sq. cm.	11.5	0.2	3.5	2.7
Treatment	Xeroform Dakin's saline	210 mgm. tyrothricin	450 mgm. tyrothricin	875 mgm. tyrothricin

Fig. 3. Infected ulcer of dorsum of left foot which did not respond to Dakin's saline or xeroform gauze dressings. During 4 weeks of treatment with tyrothricin dressings, all purulent exudate disappeared and the ulcerated area filled with granulation tissue which had almost completely epithelized. There was an almost complete disappearance of the hemolytic streptococci and a marked decrease in the number of Staphylococcus aureus.

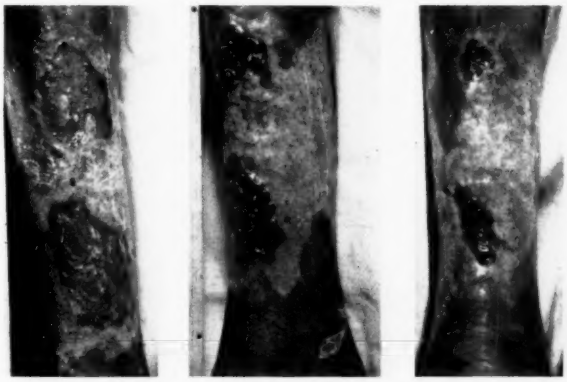


	Contro	14 days	Control	14 days
Bacteriology				
Number of colonies	60	1,200	1,800	700
Staphylococcus albus	+	+	+	0
Staphylococcus aureus	0	0	+	0
Bacillus pyocyaneus	0	0	0	+
Diphteroids	+	+	+	0
Area of wound—sq. cm.	36.2	5.0	25	16
Treatment	Dakin's saline dressings	183 mgm. tyrothricin	Saline dressings	875 mgm. tyrothricin

Fig. 4. A, An infected postoperative abdominal wound which had decreased from 36.2 to 5.0 square centimeters in 1 days of treatment with tyrothricin; bacteriological content was never significant. B, Another similar type of wound whic had granulated within 2 weeks of therapy, during which time the staphylococci aureus and albus, and diphtheroids di appeared, but Bacillus pyocyaneus developed. Both wounds epithelized completely before patients were discharged.

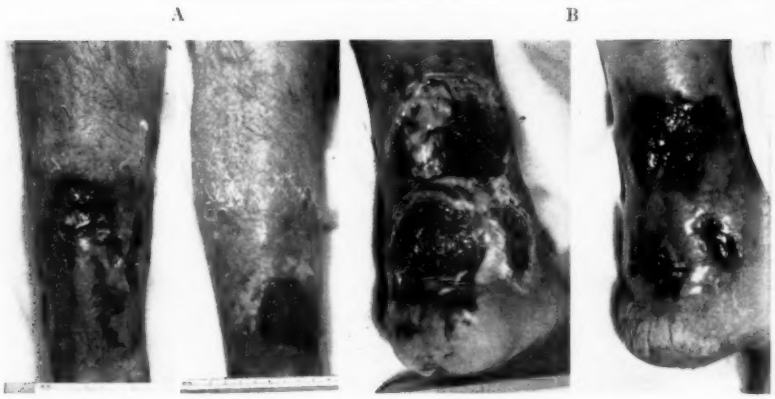
	Control	14 days	27 days
Bacteriology			
Number of colonies	6,400	1,000	100
Staphylococcus aureus	+	+	0
Bacillus pyocyaneus	+	+	+
Diphtheroids	+	0	+
Area of wound—sq. cm.	64.5	30.5	20.3
Treatment	Dakin's saline	755 mgm. tyrothricin	1,500 mgm. tyrothricin

Fig. 5. Wound separation following small bowel resection in a hypoproteinemic patient; all tissues down to peritoneum had separated and were covered with a thick purulent exudate. Within 2 weeks of treatment all exudate was cleared up and the wound was lined with healthy granulation tissue. After 27 days the wound had decreased 68 per cent in size, leaving an area of 20.3 square centimeters to be epithelized. A bactericidal effect upon Staphylococcus aureus was seen.



	Control	14 days	35 days
Bacteriology			
Number of colonies	57,000	125,520	38,400
Staphylococcus albus	+	0	0
Staphylococcus aureus	+	+	+
Bacillus pyocyaneus	0	+	+
Diphtheroids	+	0	+
Area of wound—sq. cm.	37	24.5	9
Treatment	Bismuth Potassium iodide	525 mgm. tyrothricin	1450 mgm. tyrothricin

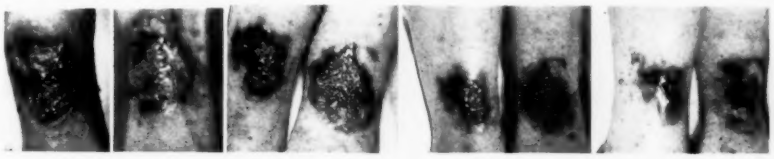
Fig. 6. Two large punched-out infected ulcers of the leg of a senile female negress which were thought to be due to lues in the opinion of the dermatological consultants. No healing was seen after 3 weeks of treatment with bismuth and potassium iodide therapy. After 2 weeks of tyrothricin the punched-out areas had completely granulated in and the surrounding skin had also improved in its appearance. Thirty-five days of tyrothricin treatment produced a 75 per cent decrease in the size of the wound with only 9 square centimeters left to be epithelized. The drug was bactericidal for the Staphylococcus albus in this case.



	Control	25 days	Control	25 days
Bacteriology				
Number of colonies	2,200	100	505,000	150,000
Staphylococcus aureus	+	0	+	<100
Bacillus pyocyaneus	0	+	+	+(104,000)
Diphtheroids	+	+	+	+
Area of wound—sq. cm.	16	15.8	80	28
Treatment	Dakin's saline	1,115 mgm. tyrothricin	Saline dressings, sulfathiazole	1,050 mgm. tyrothricin

Fig. 7. A, An infected traumatic laceration in a malnourished vagrant which had not responded to treatment with Dakin's saline solution. Twenty-five days' treatment with tyrothricin caused a complete disappearance of all necrotic tissue and exudate and complete replacement by granulation tissue. B, A decubitus ulcer due to a plaster cast which recurred several times over a period of 4 years. After 25 days' treatment with tyrothricin all necrotic tissue had disappeared in the denuded muscles and the tendons were covered by a thick layer of granulation tissue. Skin grafting was subsequently attempted but was only partially successful, presumably due to the high count of Pseudomonas pyocyaneus. A bacteriocidal effect upon Staphylococcus aureus was demonstrated in both cases.

on culture, 2,700 colonies of Staphylococcus albus in the right wound and 1,300 colonies of Staphylococcus aureus and citreus. The right wound was treated with tyrothricin for 35 days, after which time culture of the wound no longer contained Staphylococcus albus, but 1,600 colonies of pyocyaneus and 1,800 colonies of diphtheroids. The left wound was the control and after 35 days' culture of it showed 100 colonies of Staphylococcus aureus. The third case of this group was that of a secondarily infected epidermophytosis of both legs; the right leg was treated with tyrothricin and the bacteriological count, which was 200 colonies of staphylococcus and diphtheroids, rose to 13,000 colonies with the appearance of pyocyaneus. The control leg was treated with saline and the initial bacterial count of 100 colonies of Staphylococcus aureus rose to 1,000,000 colonies of Staphylococcus aureus, pyocyaneus, and diphtheroids. Case 4 of this group (Fig. 17) was another with bilateral varicose ulcers. The right wound was treated with tyrothricin for 20 days and a bacteriological count of 70,000 colonies of Staphylococcus aureus and diphtheroids changed to 576,000 colonies of pyocyaneus and diphtheroids with complete disappearance of the Staphylococcus aureus; the left wound was treated with saline and the initial bacteriological count of 1900 colonies of Staphylococcus aureus and diphtheroids rose to 1,000,000 colonies of the same organisms plus pyocyaneus. In Case 5 with bilateral decubitus ulcers, the right wound was treated with tyrothricin for 28 days during which time the count rose from 100 colonies of Staphylococcus albus and aureus and diphtheroids to 4,200 of the same flora. The left wound, treated with saline as a control, had an initial count of 20



	Contro		14 days		21 days		35 days	
	Right	Left	Right	Left	Right	Left	Right	Left
Bacteriology Number of colonies	2,700	1,300	100	24,080	100	040,000	3,100	500,000
Staphylococcus albus	+	0	+	0	0	0	0	0
Staphylococcus aureus	0	+	0	+	0	<100	0	0
Staphylococcus citreus	0	+	0	0	0	+	+	+
Bacillus pseudomonas	0	0	0	+	+	+	+	+
Area of wound—sq. cm.	40	42	20	33	12	20	40	12.5
Treatment	Dakin's saline dressings	Dakins' saline dressings	700 mgm. tyrothricin	Saline dressings	1000 mgm. tyrothricin	Unna's paste boot	1000 mgm. tyrothricin	Saline

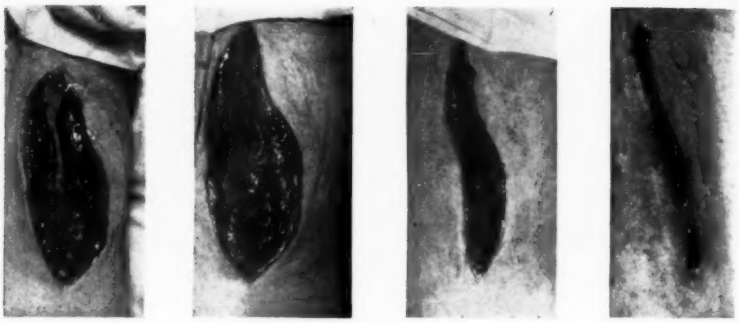
Fig. 8. Bilateral infected varicose ulcers of almost equal size which had not responded to Dakin's saline dressings. Right leg was selected for treatment with tyrothricin while left leg was employed as a control. Right leg showed a more rapid healing so that at the end of 35 days of treatment the right ulcer had decreased 90 per cent in size whereas the left ulcer had decreased 70 per cent. A more effective bacteriostatic influence was apparent in the tyrothricin treated wound than in the control.

colonies of Staphylococcus aureus and diphtheroids, which rose to 56,000 colonies of the same organisms plus pyocyaneus. The sixth case (Fig. 19) of this group was that of bilateral varicose ulcers; the right and larger wound was treated with tyrothricin for 28 days and a bacteriological count of 160,000 colonies of Staphylococcus aureus and hemolytic streptococcus changed to one of 1,000,000 colonies of pyocyaneus with complete disappearance of the staphylococcus and streptococcus. The left ulcer was treated with Dakin's saline solution with an initial bacteriological count of 172,800 colonies of the same flora as the right wound which changed to a count of 26,000 pyocyaneus and a similar disappearance of staphylococci and streptococci.

C. Hematological. Hematocrit determinations were made in 48 of the 77 patients treated at the beginning and at weekly intervals after treatment. The patients had received quantities of tyrothricin varying from 177.5 milligrams to 6,905 milligrams in a period varying from 7 to 48 days. Significant changes in the hematocrit (more than 3%) occurred in 14 of 48 cases studied; in the remainder the hematocrit varied slightly or none at all. In 14 cases where the hematocrit changed, a rise was noted in 8 and a fall in 6. There was no relationship to dose of drug administered, period of administration, type of infection, and therapeutic result. One may deduce, at least in so far as the hematocrit is a criterion, that there was no apparent hemolysis produced in these patients as the result of tyrothricin therapy.

Hemoglobin determinations were carried out in the same series of 48 patients, and changes of 2 grams per 100 cubic centimeters or more were present in 15 patients; in 6 the hemoglobin decreased and in 9 it increased. Again there was no significance in these changes. In the main, hemoglobin changes paralleled the changes in the hematocrit.

Sedimentation rates were determined in the same series of 48 patients and recorded as millimeters per hour. In all but 1 case the initial sedimentation rate was found elevated above normal. In only 1 case did the sedimentation rate fall 10 millimeters or more whereas in 8 cases it rose 10 millimeters or more. This test, as a criteria of the treatment

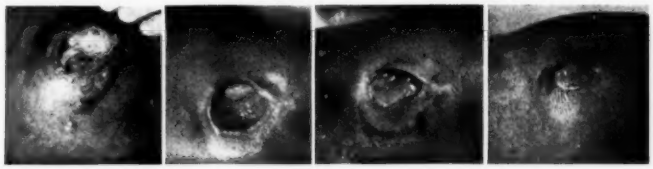


	Control	6 days	14 days	42 days
Bacteriology Number of colonies				
Hemolytic streptococcus	24,400	700	600	0
Staphylococcus aureus	1,200	100	100	0
Bacillus pyocyaneus	0	0	0	2,400
Diphtheroids	0	0	100	0
Bacillus terminalis	0	0	0	6,000
Area of wound—sq. cm.	88	67	43	14.5
Treatment	Incision and drainage	500 mgm. tyrothricin	1,300 mgm. tyrothricin	2,060 mgm. tyrothricin

Fig. 9. Abscess of the thigh which upon incision was found to extend down between the quadriceps muscles. A 1 milligram to 1 cubic centimeter solution of tyrothricin was used here and at the end of 6 days the base of the wound was completely filled in with granulation tissue and after 42 days the area still requiring epithelization was only 17 per cent of the former size of the wound. Bacteriocidal effects were noted which were similar to those previously described.

	Control	13 days	28 days
Bacteriology Number of colonies			
Hemolytic streptococcus	400	0	0
Staphylococcus aureus	18,800	100	300
Bacillus pyocyaneus	0	0	1,500
Diphtheroids	0	100	4,800
Area of wound—sq. cm.	32.2	21.4	8.4
Treatment	Saline dressings	750 mgm. tyrothricin	1,450 mgm. tyrothricin

Fig. 10. Infected traumatic lacerations in a diabetic whose leg had been previously amputated at the mid-calf level. All traces of exudation had disappeared at the end of 13 days' treatment with tyrothricin, and at the end of 4 weeks a 73.9 per cent decrease in the size of the wound had resulted, leaving only an area of 8.4 square centimeters to be epithelized. A lethal effect upon hemolytic streptococci and Staphylococcus aureus was demonstrated.

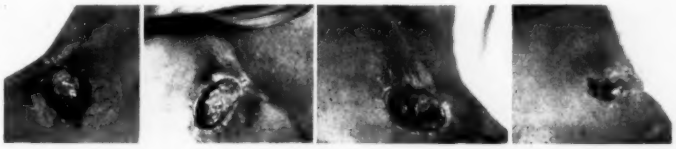


	Control	14 days	29 days	55 days
Bacteriology				
Number of colonies				
Hemolytic streptococcus	5,000	0	0	0
Staphylococcus aureus	200	500	100	0
Bacillus pyocyaneus	0	100	100	400
Diphtheroids	0	100	0	000
Area of wound—sq. cm.	18.5	12.5	6.6	4.3
Treatment	(8 mos.) Gentian violet, urea, sulfonamides, ultraviolet, Dakin's saline	825 mgm. tyrothricin	1,625 mgm. tyrothricin	2,775 mgm. tyrothricin

Fig. 11. This decubitus ulcer of the right hip of a 27 year old colored female failed to respond to a variety of therapeutic measures over a period of 8 months, during which time she was bedridden. Within 1 month of treatment with tyrothricin there was a clearance of all necrotic exudate and at the end of 55 days of tyrothricin treatment there was a 76.7 per cent decrease in the size of the wound and the patient was ambulant. A bacteriocidal effect upon the hemolytic streptococci and Staphylococcus aureus present in this case was demonstrated.

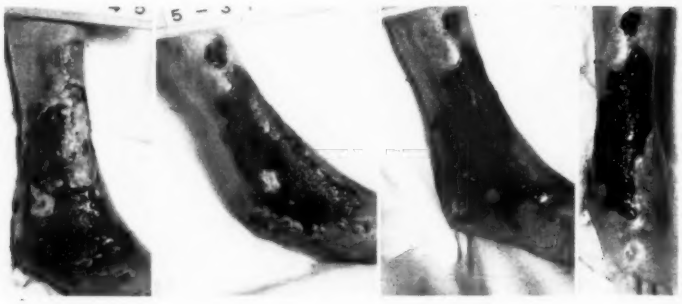
of the infection, was not of value within the period it was used.

Total serum proteins were studied with the objective in mind of eliminating hypoproteinemia as a factor in impaired wound healing and to follow the effect of infection upon hyperproteinemia. Eleven of 48 patients thus studied presented an initial total serum protein of less than 6.5 grams per 100 cubic centimeters, and 3, levels more than 8.0 grams per 100 cubic centimeters; in the course of treatment the subnormal values tended to rise to normal and the elevated ones decreased. In the group of 48, a total of 6 patients showed a



	Control	7 days	14 days	22 days
Bacteriology				
Number of colonies	96,000	3,200	2,100	12,000
Nonhemolytic streptococcus	+	0	0	0
Staphylococcus aureus	+	+	0	0
Bacillus pyocyaneus	0	+	+	+
Diphtheroids	+	+	+	+
Area of wound—sq. cm.	18	16	13	4.0
Treatment	Iodoform gauze	300 mgm. tyrothricin	450 mgm. tyrothricin	675 mgm. tyrothricin

Fig. 12. Infected wound following a saphenous vein ligation. Complete disappearance of edema and exudate with reduction of the size of the wound of 77 per cent resulted from 22 days' treatment with tyrothricin. A lethal effect upon nonhemolytic streptococci and Staphylococcus aureus is to be noted whereas pyocyaneus organisms made their appearance in the course of treatment. The patient was discharged on the 22nd day.



	Control	14 days	42 days	56 days
Bacteriology				
Number of colonies	121,000	121,800	200,000	7,300
Staphylococcus albus	+	+	+	o
Staphylococcus aureus	+	+	+	o
Bacillus pyocyaneus	o	+	+	+
Diphtheroids	o	+	+	+
Area of wound sq. cm.	185	150	90	60
Treatment	Saline dressings	3,000 mgm. tyrothricin	9,000 mgm. tyrothricin	12,800 mgm. tyrothricin

Fig. 13. Marked cellulitis of the lower leg and foot of a diabetic. This lesion was treated with a stronger tyrothricin solution (1 mgm./c.c.) which resulted in a rapid disappearance of all necrotic tissue and exudate and replacement by granulation tissue. A 67 per cent decrease in the size of this large wound occurred in 56 days, at the end of which time a skin graft was successfully performed. A pronounced lethal effect upon Staphylococcus albus and aureus was noted.

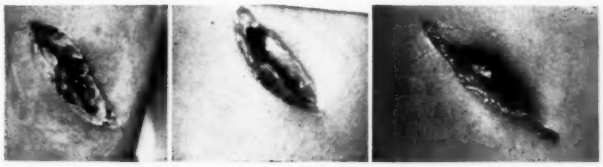
drop in total serum proteins of 0.5 gram per 100 cubic centimeters, and a similar increase in 13 patients. The most marked cases of hypoproteinemia were seen in patients with overwhelming lesions such as eviscerated abdominal wounds, empyema, and cellulitis.

In 48 patients studied, the icterus index showed a rise above normal in 2 instances. One was in a patient with Buerger's disease who received 1,000 cubic centimeters of blood after a lumbar sympathectomy. The other was in a patient with an infected burn of the trunk and arms. Neither patient showed clinical signs of jaundice; nevertheless treatment was discontinued.

D. Reactions. Only 3 instances of reaction which could be attributed to tyrothricin treatment were seen. One was in a draining thoracotomy wound following empyema; within 24 hours after the initial introduction of 15 milligrams tyrothricin in 30 cubic centimeters of distilled water into the pleural cavity, a generalized maculopapular rash occurred which was associated with intense itching and subsequent scaling. Treatment was discontinued in this case. However, 5 more chest wounds treated with tyrothricin showed no such complications. A second reaction was seen in a patient treated with 225 milligrams of tyrothricin in 450 cubic centimeters distilled water over a period of 3 days. At the end of this time the patient's leg became erythematous and warm and developed a temperature of 103.2 degrees F. This condition disappeared upon discontinuation of treatment. The third complication was seen in a patient with a huge abscess of the thigh (Fig. 9). After several weeks of treatment, a maculopapular rash developed about the wound edges. Because of the lack of subjective complaint and the excellent response in the wound, treatment was continued. The rash eventually disappeared.

DISCUSSION

In the selection of the type of lesion suitable for therapy with tyrothricin, the following considerations should be kept in mind: (1) Is the lesion an open wound? (2) Is there ade



	Control	7 days	21 days
Bacteriology			
Number of colonies			
Hemolytic streptococcus	2,000	0	0
Staphylococcus aureus	6,000	32,000	5,200
Diphtheroids	0	0	400
Area of wound—sq. cm.	26.3	15	4.8
Treatment	Catheter drainage	300 mgm. tyrothricin	900 mgm. tyrothricin

Fig. 14. Lung abscess in a 31 year old colored female treated by thoracotomy and tyrothricin irrigations and packs. Within 21 days the cavity was free of all exudate and lined with clean granulation tissue.

quate drainage? (3) Is there adequate circulation? (4) What is the bacteriological flora? (5) How acute is the infection?

Tyrothricin is an antibiotic which is suitable only for topical application, does not penetrate tissues, is not excreted, and depends upon maximal local concentration for its bacteriocidal effect. For these reasons, one cannot anticipate successful responses in lesions in which the source of infection does not communicate with the surface as in small fistulous tracts, undrained abscesses, unopened carbuncles, tendon sheath infections, and other infected lesions beneath the parietes. Furthermore, since tyrothricin is not indefinitely stable at room temperature and the best results are procured with frequent dressings, wounds for which it is best suited will be those which permit frequent changes of dressings or irrigations. For example, it would not lend itself well to a closed wound which is to heal by primary intention, or in the modern treatment of burns where infrequent dressings are regarded as desirable to minimize secondary infection. If a maximal local concentration of the drug must be maintained, it is apparent that the drug will be less effective when used solely as an irrigant. Herrell (9) found the material less effective in the treatment of sinusitis than in other lesions, but attributed the difference to more resistance on the part of the Staphylococcus aureus; however, the fact that the drug could not be retained within the sinuses for a significant length of time might also be operative. The fact that tyrothricin is hemolytic when absorbed interdicts its use in intrapleural injections in cases of closed empyemas or in peritoneal infections, for which penicillin has been recommended.

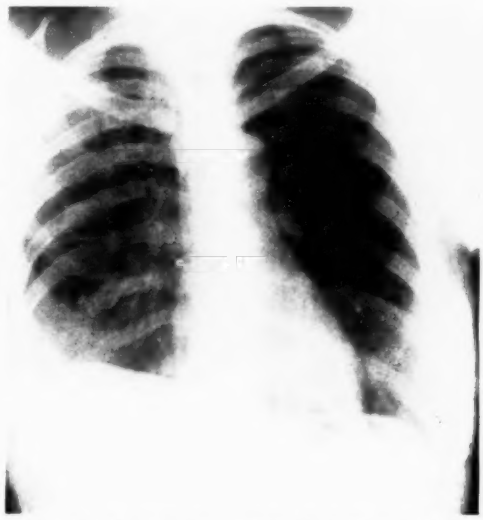
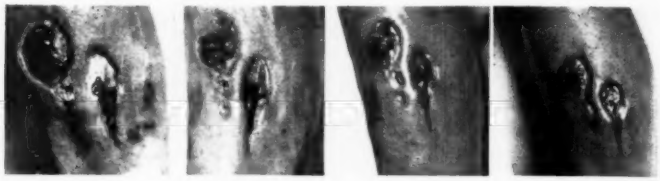


Fig. 14a. Roentgenogram of the chest after 21 days of treatment indicated the disappearance of the abscess. Hemolytic streptococci were the only organisms affected. The patient was discharged on the 21st day, completely recovered.



	Control	14 days	28 days	36 days
Bacteriology				
Number of colonies	13,000	200,000	44,000	200,000
Hemolytic streptococcus	+	+	o	o
Staphylococcus aureus	+	o	o	o
Bacillus pyocyaneus	+	+	+	+
Diphtheroids	o	+	+	+
Area of wound—sq. cm.	27.5	16	12	5.2
Treatment	Dakin's saline	600 mgm. tyrothricin	1,200 mgm. tyrothricin	1,550 mgm. tyrothricin

Fig. 15. A 57 year old diabetic who had burned himself with a hot water bottle which resulted in ulcerations; these were refractive to a large variety of therapeutic agents over a period of 3 months. The ulcer extended down to the fascia of the muscles of the leg. Satisfactory granulation of the wound began soon after tyrothricin was used, and in 36 days the patient was discharged from the hospital with a wound which had decreased 81 per cent in area. Hemolytic streptococci and Staphylococcus aureus had completely disappeared but pyocyaneus and diphtheroid organisms had increased in number.

	Control	14 days	29 days	56 days
Bacteriology				
Number of colonies	64,000	3,800	200	200
Hemolytic streptococcus	+	o	o	o
Staphylococcus aureus	+	+	+	o
Bacillus pyocyaneus	+	+	+	o
Diphtheroids	+	+	+	+
Gram anaerobe (Bacillus welchii group)	+	+	o	o
Area of wound sq. cm.	45	40	25	6
Treatment	Saline dressings	1,200 mgm. tyrothricin	2,125 mgm. tyrothricin	4,050 mgm. tyrothricin

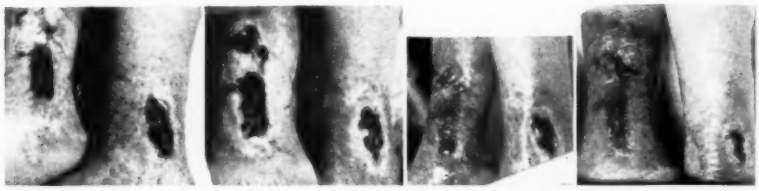
Fig. 16. Infection of a wound following operation for a strangulated inguinal hernia requiring a bowel resection. A edema and exudate had disappeared within 2 weeks of tyrothricin treatment but it required 56 days to completely gra ulate and epithelize the wound. The reduction in size of the wound was 86 per cent. A bacteriocidal effect upon hemolyt streptococci, Staphylococcus aureus, Bacillus pyocyaneus, and anaerobe of the Bacillus welchii group was demonstrate

	Control		13 days		20 days	
	Left	Right	Left	Right	Left	Right
Bacteriology						
Number of colonies	1,900	70,000	1,000,000	1,000,000	280,000	576,000
Staphylococcus aureus	+	+	+	+	+	o
Bacillus pyocyaneus	o	o	+	+	+	+
Diphtheroids	+	+	+	+	+	+
Area of wound sq. cm.	7.4	36.1	3.0	1.0	2.0	o
Treatment	None	None	Saline	550 mgm. tyrothricin	Saline	800 mgm. tyrothricin

Fig. 17. Bilateral stasis ulcers in a 62 year old negro female. The larger wound was treated with tyrothricin and was completely filled in by granulation tissue which required epithelization; a lethal effect upon the Staphylococcus aureus in this wound was shown but there was a marked increase in Bacillus pyocyaneus and diphtheroids. The smaller wound was treated with saline, decreased 73 per cent in size, and still contained Staphylococcus aureus at the end of treatment.

	Control	14 days	22 days	35 days
Bacteriology				
Number of colonies	480,000	108,000	400	64,000
Hemolytic streptococcus	+	+	o	o
Staphylococcus aureus	o	+	+	o
Bacillus pyocyaneus	o	+	+	+
Diphtheroids	o	+	+	+
Area of wound—sq. cm.	39	80	45	36
Treatment	Amputation	Débridement 2,250 mgm. tyrothrycin	4,350 mgm. tyrothricin	6,200 mgm. tyrothricin

Fig. 18. Infected amputation stump treated by débridement and tyrothricin. All necrosis disappeared, the denuded muscle was covered over by granulation tissue which produced a 55 per cent decrease in the size of the wound and spared the patient the necessity for reamputation. A disappearance of hemolytic streptococci and Staphylococcus aureus was seen whereas Bacillus pyocyaneus and diphtheroid made their appearance in the course of treatment.

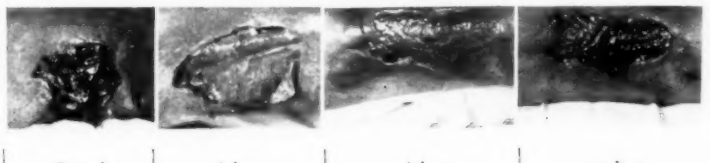


	Control		6 days		14 days		28 days	
	Right	Left	Right	Left	Right	Left	Right	Left
Bacteriology Number of colonies	160,000	172,000	1,000,000	806,000	1,000,000+	51,400	1,000,000+	26,000
Hemolytic streptococcus	+	+	+	+	0	0	0	0
Staphylococcus aureus	+	+	+	+	0	0	0	0
Bacillus pyocyaneus	0	0	+	0	+	+	+	+
Diphtheroids	0	+	+	+	0	+	0	0
Area of wound—sq. cm.	21	13	22	8.6	9.5	6.1	9.1	2.5
Treatment	Heat lamp Dakin's sal.	225 mgm. tyrothricin	Dakin's saline	525 mgm. tyrothricin	Dakin's saline		1,300 mgm. tyrothricin Dakin's saline	

Fig. 19. Bilateral varicose ulcers which had been repeatedly treated over a period of years. The tyrothricin treated ulcer (right) was the larger but granulated in the same period of time as the smaller lesion. The lesions demonstrated bacteriocidal effects on the same organisms.

The surgical principles of the treatment of pus under pressure were adhered to in this study. In every instance adequate drainage or débridement was carried out; first, to avoid the destructive effects of pus under tension, and second, to increase surface contact between the medicament and the wound.

Tyrothricin was always used following such drainage and never in place of it. With the poor penetration power of tyrothricin, this principle will apply even more. Neither exudate nor necrotic tissue appeared to interfere with the action of tyrothricin; in many instances areas of necrosis were replaced by



	Control	8 days	36 days	50 days
Bacteriology Number of colonies				
Hemolytic streptococcus	62,800	121,000	0	0
Staphylococcus aureus	0	6,400	100	0
Bacillus pyocyaneus	1,200	0	1,200	400
Diphtheroids	0	0	1,300	500
Area of wound—sq. cm.	80	75	61.5	46
Treatment	Incision and drainage	1,750 mgm. tyrothricin	5,950 mgm. tyrothricin	9,200 mgm. tyrothricin

Fig. 20. Popliteal abscess which was treated by incision and tyrothricin dressings. The defect extended down to the muscular compartments, but in 50 days of tyrothricin treatment, all exudate had been cleared and the wound sufficiently well granulated for skin grafting. Here again a bacteriocidal effect upon hemolytic streptococci and Staphylococcus aureus was shown.

granulation tissue without the aid of débridement.

An adequate blood supply was found to be as essential with this method of treating wounds as with all others. Every case in which the infected wound was associated with an impoverished blood supply, such as Buerger's disease, and arteriosclerotic gangrene, showed clinical failure. In fact it appears that one of the reasons for the high rate of excellent results with infected postoperative abdominal wounds was the relatively large blood supply in such areas, in contrast to the relatively poor supply in lesions of the extremities. All this implies that tyrothricin can only augment the ability of the body to ward off an infection and that an adequate blood supply is necessary to mobilize the factors of resistance and the proper nutrient substances.

It is important to determine the bacterial flora of the lesion before proceeding with tyrothricin therapy even though most of these infected wounds contain staphylococci. The nature of the predominant bacterium found gives some prognostic information. Our results demonstrate the greater effectiveness of tyrothricin upon hemolytic streptococcus, Staphylococcus aureus, and the Staphylococcus albus in the order named, and little effect upon all others. The presence of a predominantly gram negative infection, such as pyocyaneus and coliform organisms militates against the use of this drug. Finally, since the progress of the wound from a clinical point of view has been found to correlate well with the disappearance of the most pathogenic organisms, repeated bacteriological cultures would aid in checking the progress of treatment.

Acute infections differ from chronic infections in many respects which are of importance in the response to any treatment. Acute infections are more apt to be superficial, to be spread over a wider surface area, to be surrounded by less connective tissue,to contain exudate with pathogenic bacteria, and to produce symptoms which attract early treatment. In contrast, chronic infections are usually more localized, surrounded by a less permeable layer of granulation tissue, contain more necrotic tissue, are more apt to contain a variety of organisms and to leave the patient in a debilitated condition. Upon theoretical grounds, then, an acute infection should respond better to treatment with tyrothricin than a chronic one; this was actually found to be true.

From the frequency of the growth of pyocyaneus in these wounds it would appear that this organism, which is normally a saprophyte, is given a chance for greater growth after the streptococci and staphylococci have been destroyed. Although the organism is usually nonpathogenic there is evidence that it interferes with successful skin grafting. In this series two skin grafts which were only 50 to 60 per cent successful had high bacteriological counts of pyocyaneus (Fig. 7B), while 2 cases without significant numbers of pyocyaneus organisms had 90 per cent or better "takes" (Figs. 1 and 20).

CONCLUSIONS

1. Tyrothricin was used as a wet dressing in the treatment of 77 patients with surgical infections, the majority of which had failed to respond to previous methods of treatment. (a) Fifty of the 77 patients (65 per cent) had excellent clinical results. (b) Eight of the 77 patients (10 per cent) had fair clinical results. (c) Nineteen of the 77 patients (25 per cent) had poor clinical results.

2. Tyrothricin, when used on one of the bilateral lesions in 6 cases, produced in 5 either a more rapid rate of healing, less pain and exudate, or a greater bacteriocidal effect than control measures in the contralateral lesion.

3. Tyrothricin was most effective in hemolytic streptococcal lesions, next in those with staphylococcus aureus and albus. It was ineffective when the preponderant organisms were gram negative.

4. Tyrothricin appeared to encourage the growth of Bacillus psuedomonas, pyocyaneus, and diphtheroid organisms.

5. Tyrothricin was not found to produce anemia or hemolysis in the type of lesions studied.

6. Tyrothricin treatment was associated with mild skin reaction in 3 patients; these reactions disappeared when treatment was discontinued in 2 instances, and in spite of continuation of therapy in the third.

7. Tyrothricin is recommended as a nontoxic, noninjurious antibiotic agent for local use in the treatment of surgical infections, if these meet the following criteria: (a) the wound is open, (b) there is adequate surgical drainage, (c) there is adequate blood supply, (d) the predominant organisms are streptococci or staphylococci or both.

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THE IDENTIFICATION OF CLOSTRIDIUM WELCHII IN MIXED CULTURES AND DÉBRIDED TISSUE AND DETERMINATION OF SENSITIVITY OF THE ORGANISM TO PENICILLIN

GEORGE HELLER, Captain, Sn.C., A.U.S., Brooklyn, New York, MONROE E. FREEMAN, Major, Sn.C., A.U.S., NATHANIEL H. SHOPE, Technical Sergeant, Medical Department, A.U.S., ROBERT H. KINDRICK, Technical Sergeant, Medical Department, A.U.S.

DURING recent military operations in Europe, this laboratory received a large number of mixed cultures from the débrided tissue of battle wounds; the majority of these contained Clostridium welchii. Although the diagnosis of gas gangrene is essentially a clinical problem, Altemeier pointed out that dressings, casts, and splints make observations so difficult that gas gangrene developing under a cast may escape detection for 48 to 72 hours. Because of these difficulties a rapid bacteriological method for identifying gas gangrene organisms may be an aid in the management of contaminated wounds.

A number of rapid bacteriological methods for the identification of Clostridium welchii have been employed. But they have certain disadvantages for use in forward military installations. The procedures of Altemeier and Fels depend on the production of "stormy fermentation" in milk. However, Reed and Orr as well as ourselves have found a number of toxigenic strains of Clostridium welchii which failed to produce "stormy fermentation" under prescribed conditions. Moreover, other nonpathogenic Clostridia which produce "stormy fermentation" are frequently found in wounds.

Nagler and Hayward employed methods based on the splitting of insoluble fatty material in human serum by welchii toxin and the specific inhibition by welchii antitoxin. This test done on agar plates (5) appears to be quite reliable except in the presence of Bacillus proteus which causes a diffuse opacity thus interfering with the reading of the opaque zone produced around the welchii colony by the toxin. The necessity of employing an overnight incubation period together with special anaerobic equipment and reagents renders this method impractical for forward medical installations.

Humphreys observed that his strains of Clostridium welchii (50 in all) produced acrolein from glycerol. Since a wide variety of common aerobes and anaerobes did not give this reaction, he suggested that this test might be considered diagnostic for Clostridium welchii. Although Voisenet described a gram negative bacillus isolated from water and wine in "bitter disease" (Bacillus amaracrylus) which produced appreciable amounts of acrolein from glycerol, the incidence of this organism is rare and we have failed to encounter it in several hundred specimens from wounds. Thus the acrolein method as described by Humphreys may still be considered diagnostic for Clostridium welchii in cultures of wound specimens.

The production of acrolein from glycerol has been used in our laboratory as the basis for a rapid test for Clostridium welchii. This procedure depends upon: (1) the aerobic growth of anaerobes in a specially prepared medium; (2) the development of acidity which determines the testing time for acrolein; and (3) the testing for acrolein in the culture medium with a standardized Schiff's reagent. It is believed that this method is sufficiently simple and of short enough incubation period to be of value in forward medical installations. Since penicillin therapy is extensively used at present in gas gangrene, the procedure was ampli-

From the First Medical General Laboratory, United States Army.

fied to include a means of determining the penicillin sensitivity of Clostridium welchii in mixed cultures and débrided tissue. The inhibition of acrolein by the penicillin in the medium was taken as a measure of penicillin sensitivity.

METHODS

The methods of preparing the medium and reagents and the procedure for the detection of traces of acrolein, the production of which is specific for Clostridium welchii, are given in detail in the following:

A. Medium.

1. Mix distilled water.....970 milliliters
   Glycerine..... 30 milliliters
   Tryptone (Bacto)..... 20 grams
   Sodium chloride (C.P.). 5 grams
   Agar..... 2 grams
2. Heat to boiling until fully dissolved.
3. Add 5 grams ascorbic acid (C.P.)
4. Adjust to *p*H 6.8 with 5N NaOH (about 5.0 to 5.3 ml. is required)
5. Add 7.5 milliliters of brom cresol purple solution, prepared as follows:
   Distilled water..... 99 milliliters
   N/10 NaOH..... 1 milliliter
   Brom cresol purple..100 milligrams
6. Dispense measured volumes (100 ml.) in screw capped bottles, fill almost completely so as to give the smallest surface exposure to air.
7. Sterilize in Arnold for 30 minutes on 2 successive days.
8. Final *p*H should be approximately 6.8
   Final Eh should be approximately −0.150 volt.
9. Add enough penicillin aseptically to some of the bottles of medium to make 1 Oxford unit per milliliter. No depreciation of penicillin potency in the medium has been observed for at least 2 weeks when it is stored in a tightly screw-capped bottle and refrigerated.
10. The medium with or without penicillin should be stored at about 5 degrees C.

B. Modified Schiff's reagent.

The smallest amounts of acrolein produced by Clostridium welchii in the glycerol medium were detected by a modified Schiff's reagent. In order to obtain consistent and reproducible results, it was necessary to standardize each batch of stock reagent against known concentrations of an aldehyde. Satisfactory results were obtained with reagents that gave a negative test (yellow color) with formaldehyde solution (U.S.P.) diluted 1:250,000 with the medium described; a faint positive test (light pink color) with formaldehyde at 1:125,000 dilution, and a strongly positive test (deep pink color) with formaldehyde diluted 1:75,000.

The stock unstandardized solution of Schiff's reagent remained stable for a month when stored in a glass stoppered brown bottle at room temperature in the dark. This solution was prepared as follows:

0.25 gram of basic fuchsin was dissolved (by heating if necessary) in 100 milliliters of distilled water and cooled to room temperature. Small insoluble residues were discarded. Fifty milliliters of *freshly* prepared 4 per cent sodium sulfite and 4 milliliters of concentrated hydrochloric acid were added immediately. Distilled water was added to a total volume of 250 milliliters. After standing 5 minutes at room temperature, the solution was filtered rapidly through a large fluted filter paper.

Sensitivity of the stock solution could be affected by varying the concentration of basic fuchsin or sodium sulfite. The most satisfactory standardized solutions were obtained by determining the amount of concentrated H_2SO_4 necessary to be added to stock solution to give the reactions mentioned above with the given concentrations of formaldehyde in medium. The requisite amount of sulfuric acid was determined for each batch of unstandardized reagent. Standardized stock solution was found to be unstable. It was necessary to add the required amount of concentrated H_2SO_4 to stock solution sufficient only for the tests at hand.

The titration method employed for the standardization of stock reagent was as follows:

The formaldehyde-media solutions were made by the usual methods of serial dilution. One milliliter of formalin (37–40% formaldehyde U.S.P.) was pipetted into 9 milliliters of medium and thoroughly mixed. One milliliter of this solution was pipetted into 9 milliliters of medium etc. Dilutions of 1:30,000, 1:50,000, and 1:100,000 of formalin in medium were chosen. These dilutions of formalin correspond to formaldehyde concentrations of approximately 1:75,000, 1:125,000, and 1:250,000, respectively.

To adjust the stock solutions to optimum sensitivity for tests, 0.075 milliliter of concentrated H_2SO_4 was added to a 10 milliliter portion of the stock solution of Schiff's reagent. One milliliter of this acidified reagent was added to 1 milliliter of each of the formaldehyde-medium dilutions and allowed to stand for 20 minutes. If this amount of sulfuric acid produced the optimum sensitivity, the 1:250,000 formaldehyde-medium dilution remained negative (yellow color); the 1:125,000 formaldehyde dilution

TABLE I.—RESULTS OF TESTS FOR THE IDENTIFICATION OF CLOSTRIDIUM WELCHII AND ITS SENSITIVITY TO PENICILLIN

Type of specimen cultured[1]	Number of specimens cultured	Methods of identifying Clostridium welchii						Other organisms present[4]
		Acrolein test				Nagler test[2]	Routine cultural methods[3]	
		Tube No. 1	Tube No. 2		Average No. hrs. incubated before testing	Number positive	Number welchii confirmed	
		Plain medium	Plain medium with 1 Oxford unit Penicillin per ml.					
		Number positive	Number negative	Number positive				
Mixed cultures	111[5]	69	62	7	4[1/2]	69[7]	69	See notes
Tissue	10[6]	0	0	0	3	0	0	
Pure cultures	27	27	27	0	4	0	0	None

[1]Mixed cultures were secondary transplants of wound tissue cultures. Pure cultures of Clostridium welchii were isolated from tissue cultures and sent to laboratory for confirmation. Tissues were débrided tissue from wounds.

[2]Nagler test: Toxigenic Clostridium welchii produce marked zones of opacity around colony on 20 per cent human serum proteose No. 3 (Bacto) agar plates which do not appear when welchii antitoxin is present.

[3]After Reed and Orr, based on cultural and biochemical characteristics.

[4]Combinations of 2, 3, or 4 other aerobes and anaerobes found in mixed cultures and tissue cultures.

[5]42 of the mixed cultures were negative for Clostridium welchii by all tests indicated in Table I.

[6]4 of the tissue cultures were negative for Clostridium welchii by all tests indicated in Table I.

[7]Includes 4 doubtful results due to presence of Bacillus proteus which produced diffuse opacities over entire plates.

[8]Organisms identified by routine cultural methods were: Staphylococcus albus and aureus; Streptococcus hemolyticus, also viridans and nonhemolytic varieties; Bacillus proteus; Bacillus subtilis; Escherichia coli; Aerobacter aerogenes; Klebsiella friedlanderi; diphtheroids; Clostridium sporogenes, bifermentans, aerofetidum, tetanomorphum, unidentified nonpathogenic clostridia, oedematiens, septicum, histolyticum, sordellii, tetani.

became pale pink, and the 1:75,000 dilution became deep pink in 20 minutes. If the 1:250,000 formaldehyde tube turned pink in 20 minutes, the reagent was too sensitive and a new trial was made using more concentrated sulfuric acid (e.g. 0.1 ml.) in 10 milliliters of stock reagent. If both the 1:250,000 dilution and the 1:125,000 dilution remained yellow, the reagent was not sensitive enough, and a smaller amount of sulfuric acid was tried (0.05 ml. conc. H_2SO_4 to 10 ml. of stock solution).

C. *Procedure for identifying Clostridium welchii and determining its sensitivity to penicillin.*

1. Two milliliter portions of the medium, with or without penicillin, were pipetted into sterile Wassermann tubes just before use. Two tubes were used for each specimen. Tube 1 contained the plain medium, tube 2 contained the medium with 1 Oxford unit of penicillin per milliliter. A control tube was included with each batch of tests. This consisted of uninoculated medium which was used in order to check the sensitivity of the stand rdized reagent used in the test.

2. Tubes 1 and 2 were inoculated with approximately the same amounts of inoculum and mixed carefully without introducing bubbles. The inoculum consisted of 5 to 10 millimeter pieces of freshly excised tissue, blotted free of blood, or 0.1 milliliter of mixed or pure freshly grown culture.

3. Tubes 1, 2, and the blank control were incubated *aerobically* at 37 degrees C. and observed at *hourly* intervals until sufficient growth had occurred to produce an acid reaction. The time for testing for acrolein was determined by the development of a decided yellow color in tube 1. This averaged 4 to 6 hours.

4. Following the necessary period of incubation, the tubes were centrifuged at 2500 revolutions per minute for 5 minutes. One milliliter of supernatant liquid was decanted from each tube into clean sterile tubes and labelled. One milliliter of "standardized" Schiff's reagent was added to each tube and mixed well. The tubes were shaken occasionally and observed for development of pink to purple color at the end of 20 minutes.

RESULTS

Clostridium welchii were identified in mixed cultures, pure cultures, and tissue by: (a) the acrolein test described herein, (b) the Nagler

TABLE II.—RESULTS AND INTERPRETATION OF THE ACROLEIN TEST FOR CLOSTRIDIUM WELCHII AND ITS SENSITIVITY TO PENICILLIN

Tube No.	Type of supernatant		Color[1] reaction with Schiff's reagent	Interpretation		
	Media	Inoculum		Presence of Clostridium welchii	Sensitivity to penicillin	Remarks
Control	Plain	None	Pink to purple			Reagent must be re-standardized and test repeated
			Yellow			Reagent satisfactory
1	Plain	Pure culture or mixed culture or tissue	Pink to purple	Present		
			Yellow	Absent		
2	1 Oxford unit of Penicillin per 1 ml of plain medium	Pure culture or mixed culture or tissue	Yellow	Present	Sensitive	(Provided that Tube 1 is pink to purple)
		Pure culture	Pink to purple	Present	Resistant	
		Mixed culture or tissue	Pink to purple	Present	Undetermined[2]	

[1]The presence of any shade of color from pink to purple is regarded as a positive test for acrolein, provided that the uninoculated control remains yellow during the prescribed 20 minutes.

[2]Clostridium welchii may be resistant to penicillin or it may be sensitive. In the latter instance the positive acrolein reaction may be due to destruction of penicillin by other organisms present.
Actual sensitivity must be determined in the above test with a pure culture.

test, and (c) routine cultural methods, as shown in Table I. All cultures of specimens which were found to contain Clostridium welchii by the Nagler test and the routine cultural methods gave a positive test for acrolein in the glycerol media, after approximately 4 hours' incubation. Cultures that proved to be negative for Clostridium welchii by the Nagler test and the routine cultural methods failed to produce acrolein in glycerol media after 24 hours' incubation. In glycerol medium containing 1 Oxford unit of penicillin per milliliter, 95 of the 102 cultures containing Clostridium welchii gave a negative test for acrolein. In order to correlate the inhibition of acrolein production with penicillin sensitivity, 10 pure cultures of Clostridium welchii obtained from the group of 95 were also tested by the filter paper disc method of Vincent and Vincent. The results obtained from these tests showed that the growth of all strains of welchii tested were inhibited by the penicillin in blood agar plates. It would appear that inhibition of acrolein production could be used as an indicator of the penicillin sensitivity of Clostridium welchii.

Seven of the remaining mixed cultures when tested in glycerol medium containing penicillin gave a positive reaction for acrolein. However, when the pure cultures of Clostridium welchii from these seven mixtures were likewise tested, they gave a negative reaction for acrolein. Furthermore these pure cultures were inhibited by 1 Oxford unit of penicillin per milliliter of blood agar (filter paper disc method of Vincent and Vincent). This positive reaction for acrolein in the mixed cultures might be explained by the presence of Escherichia coli or Bacillus subtilis either alone or in combination (See Table I). These organisms have been described as penicillinase producers by Ungar and Bondi and Dietz (2, 3). While we did not test for the production of penicillinase *per se*, these results would indicate that such substances were produced in the mixtures, destroying the penicillin in the medium and thus permitting the Clostridium welchii to proliferate and split the glycerine to acrolein. The inactivation of penicillin in mixed cultures by nonpathogens suggests that a similar action may occur at the wound site if contaminated with the same type of bacterial flora. It should be noted however that over 93 per cent of the mixed cultures containing Clostridium welchii in penicillin medium gave a negative reaction for acrolein, indicating that most of the nonpathogens encountered were probably nonpenicillinase producers.

The degree of penicillin sensitivity was further demonstrated by the following method. A pure culture of Clostridium welchii in chopped meat broth or Brewer's thioglycol-

late medium was tested in the same manner. As a control, the filter paper disc method of Vincent and Vincent was run. Freshly grown cultures were inoculated into portions of medium containing serial dilutions of penicillin so that the final concentrations of drug were 1 Oxford unit, 0.5, 0.25, 0.125, 0.06, 0.03, 0.015 unit per milliliter of medium. Final concentration of inoculum was 1:100. A tube of medium without penicillin was also inoculated with the same amount of culture. An uninoculated blank control was run as part of the test. All the tubes were incubated and tested for acrolein as soon as the plain medium culture had turned deep yellow. The incubation period was usually about 5 hours. The smallest concentration of penicillin which inhibited the formation of acrolein was considered as an indicator of the degree of sensitivity of the test organism to penicillin.

Tests of 10 strains of Clostridium welchii for relative sensitivity to penicillin by the method described showed that 1 strain was sensitive to 0.03 unit of penicillin, 3 strains were sensitive to 0.06 unit, 3 strains were sensitive to 0.12 unit, 2 strains were sensitive to 0.25 unit, and 1 strain was sensitive to 0.5 unit of penicillin. Two of the strains tested (sensitive to 0.06 unit and 0.25 unit, respectively) were retested on two other occasions with the same results. Since an extensive series of tests have not been carried out yet, no attempt has been made to estimate the limits of experimental error in this technique.

Interpretation of the results of the test given is contained in Table II.

SUMMARY

1. A method is described for the identification of Clostridium welchii in mixed cultures, pure cultures, and wound débridement which requires no anaerobic apparatus and is completed in an average of 4 to 6 hours.

2. The test depends on the production of acrolein which in this case is considered diagnostic for Clostridium welchii.

3. A procedure is also given for determining the penicillin sensitivity of Clostridium welchii in the above types of cultures.

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REPAIR OF VESICOVAGINAL FISTULA CAUSED BY RADIATION

GRAY H. TWOMBLY, M.D., and VICTOR F. MARSHALL, M.D., F.A.C.S.,
New York, New York

THE cure of vesicovaginal fistulas has always excited the ingenuity and taxed the skill of the surgeon. Within this class of cases, those fistulas which are the result of radiation therapy, usually to the cervix or uterus, constitute a peculiarly difficult problem. There are several reasons for this:

First, the blood supply of the tissues locally is precarious as a result of the vascular radiation damage. Indeed, this is the main underlying cause of the fistula. Further, trauma may well produce more sloughing and any effort by the surgeon to correct the condition may end in a larger fistula and more fibrosis. Even if no actual slough occurs, healing of heavily radiated tissues is notoriously uncertain.

Second, such excessively fibrosed tissues are usually quite inelastic. This fibrosis extends for a few centimeters, at least, from the opening proper, and very often the whole area is massively affected. In methods where coaptation of the fistula edges is necessary, a recognized *sine qua non* to success is the absence of tension. Coaptation is difficult in the postradiation case and may be impossible.

Third, the fibrosis itself makes dissection very difficult, particularly if it is desired to raise several flaps for a multilayer closure. Postradiation fistulas often have very thin but very tough edges.

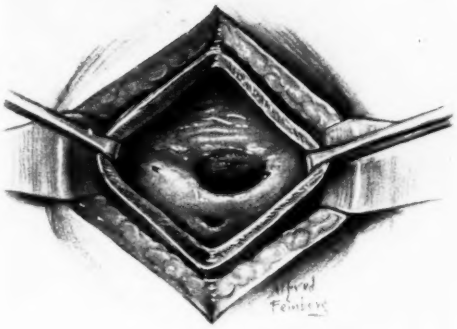
Fourth, one, or both, of the ureteral orifices are frequently within the fistula margin. In our cases, the left ureteral orifice was within the fistula wall in every one, and the right orifice always very near it. In such instances, to raise flaps or cut off the inner edge of the fistula would cut off at least one ureter and necessitate reimplantation of one or both ureters into a new portion of the bladder—a procedure adding greatly to the difficulty and length of the operation. Furthermore, after heavy radiation fibrosis (and its associated infection) it may be nearly impossible to dissect up the ureter for reimplantation (as in our Case 2).

Our 3 patients all had vesicovaginal fistulas as the result of therapy for cervical cancer. All were heavily radiated with both radium and x-ray. In each instance, the upper vagina and parametrial tissues were tough and inelastic, like heavy leather. The fistula margins were thin and fibrous. One patient had been seen by various consultants for 8 years all of whom had agreed that no method of closure could succeed for the reasons just enumerated.

DESCRIPTION OF OPERATION

Through a suprapubic incision, the space of Retzius is entered. The bladder is identified and, after the peritoneum has been pushed upward off the dome, a liberal cystotomy is carried out in the higher portions of the exposed bladder wall. The high position is chosen so that at closure the cystotomy catheter will be placed away from the symphysis, at a distance from the urethra and also from the site of the fistula repair. Closure at the desired later time occurs more rapidly with a high cystostomy than with one placed low. The interior of the bladder is exposed by retractors, and the fistula is inspected from above. Ureteral catheters are inserted since, by knowing exactly where the ureteral orifices are, damage to them can be completely avoided throughout remainder of the operation. The only sutures used in their vicinity are placed there under direct vision.

One of the assistants puts his finger in the rectum and pushes the posterior vaginal mucosa up against the fistula. A long handled scalpel with a small blade is used to mark out, transvesically, the pattern of posterior vaginal mucosa corresponding to the size, shape, and location of the fistula opening. The



ig. 1. Appearance through the suprapubic cystotomy.

Fig. 2. Sagittal section showing how the posterior vaginal wall is pushed up against the fistula.

ureteral catheters are left in place and sterile drapes are placed over the suprapubic wound.

The patient is now arranged in the lithotomy position and the vagina and perineum are prepared and draped. The interior of the vagina is exposed and the upper third is denuded of its mucosa by sharp dissection except that the previously outlined patch on the posterior vaginal wall is left undisturbed. Moderate bleeding is encountered, but with the exception of a few easily identified larger vessels which are ligated with plain catgut, bleeding usually ceases spontaneously, or after brief packing. The posterior third of the vagina to a point about 2 centimeters in front of the fistula is now a raw surface except the previously noted patch. The external edges of this excision are sutured together with interrupted chromic catgut transversely (parallel with the operating room floor), the anterior vaginal mucosa being sutured to the posterior mucosa at the margin of the dissection. Interrupted sutures are used so that some drainage may occur between the sutures from the fairly large raw surfaces above. No drain or vaginal packing is used.

The patient is then returned to the original dorsal position. With a long needle holder and long toothed forceps, interrupted chromic catgut sutures are placed at 1 centimeter intervals through the full thickness of the fistula margin about 0.5 centimeter from the actual edge of the opening and through the edge of the posterior vaginal wall patch. Four to six such sutures are usually required. At the posterior edge of the opening, there is usually a small area not requiring sutures because that edge of the patch is usually continuous with the fistula edge without any pocket intervening. If such a pocket were present, the suturing would be continued all around. During this suturing, the ureteral orifices are always in complete view, and care is taken not to place sutures too close to them. These sutures are tied just tight enough to make the patch and fistula edges touch because anything more than this might injure blood supply and allow cutting through of the sutures. In this manner, the patch is accurately fitted in place to form a floor to the fistula which is only barely depressed below the general level of the bladder base.

The cystotomy is closed with a continuous plain catgut suture through all layers of the bladder wall. This suture line is then inverted with interrupted chromic catgut mattress sutures through the outer layers of the wall. A mushroom type catheter, No. 22 to 28 size, French, is placed in the highest portion of the incision. Just above the site of the catheter, a chromic catgut suture is passed through the bladder wall, avoiding the mucosa, and each end is then put through the recti and fascia at a slightly higher level. When this suspending suture is tied, during the closure of the abdominal wall, the cystostomy site is thus held

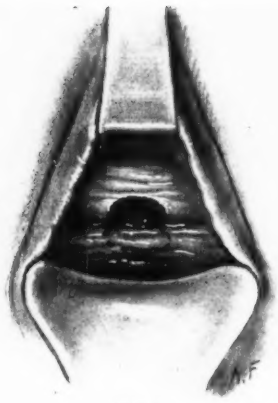


Fig. 3.

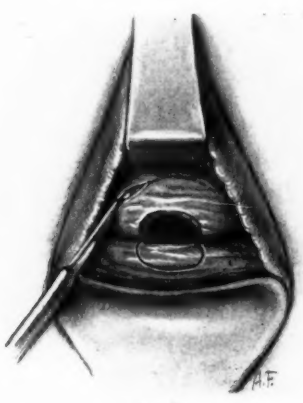


Fig. 4.

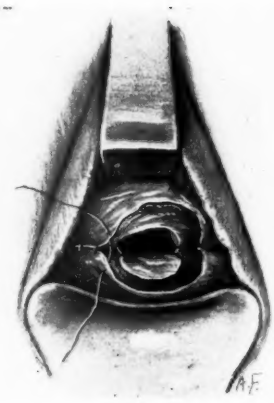


Fig. 5.

Fig. 3. Vaginal view after patch has been outlined from above.

Fig. 4. Beginning removal of the vaginal mucosa.

Fig. 5. Transverse closure of external margins of excision. Patch still in place. (Actually the excision of vaginal mucosa is somewhat more extensive than illustrated.)

high and against the recti. Also, some bulwark is created to hold the peritoneum away from this newly formed fistula tract. The wound is closed in routine fashion and the catheter is securely fastened to the skin with adhesive.

Upon return to bed, the patient is kept abdomen down as long as she will tolerate it, up to 10 days. The suprapubic tube is very gently irrigated with solution G[1] twice daily, or more often if necessary, to insure its patency —solution G decreases precipitation of urinary salts in the tube or in the suture line. Under no circumstances is this tube closed even for a short while. The addition of low pressure, "bubble", suction is, we believe, an advantage. If the patient cannot tolerate the prone position, the "bubble" suction is probably adequate if cared for. This low pressure suction is continued for over 2 weeks after operation and the patient is then placed on straight drainage for 2 days. After this, the tube is removed and voiding usually begins in a few hours. After the suprapubic area has been dry for 24 hours, the patient is discharged. During the convalescence, a daily gentle flush of the vaginal vestibule is done with a mild antiseptic. Care is taken to introduce nothing against the vaginal suture line which might separate it. The catgut vaginal sutures, also those in bladder, come out spontaneously.

We hope that it is readily apparent from the description given that there are two suture lines plus an adhering area of raw surfaces at least 2 centimeters wide closing the fistula. The safety from damage to the ureters should be stressed. Adequate bladder drainage without a urethral catheter is of great importance, particularly during the healing period. In our cases, the uterus and cervix already were either removed or obliterated by radiation but, if there were any question of continued uterine function, a hysterectomy would be necessary before this operation could be done.

[1]Citric acid (monohydrous) ..... 32.3 gm.
Magnesium oxide (anhydrous) ..... 3.8 gm.
Sodium carbonate (anhydrous) ..... 4.4 gm.
Distilled water ad ..... 1000 c.c. (10)

CASE REPORTS

CASE 1. Mrs. A. P. No. 70622. This 34 year old female first entered Memorial Hospital on May 20, 1943, with cancer of the cervix classified as League of Nations, stage II, because it extended into the left parametrium a short distance. It was freely movable, however. A biopsy showed epidermoid carcinoma, grade II.

The patient was treated by what was the routine treatment for cancer of the cervix at that time. This consisted of roentgen therapy, 250 r to a large 14 by 19 centimeter anterior port the first day, a similar treatment to a 14 by 19 centimeter posterior port the second day, and two treatments of 250 r each to 11 by 11 centimeter right and left lateral ports the third day. The cycle was repeated until each port had received 1750 r. The factors were 200 kilovolts, peak

0.5 millimeter copper filter, 70 centimeter target skin distance, 30 milliamperes. On conclusion of the external roentgen therapy, treatment was given to the cervix through vaginal cones. This consisted of 4 treatments of 500 r each through a 4 centimeter cone to the cervix direct and 4 treatments of 750 r each to each fornix through 3.5 centimeter cones. One treatment was given daily. The factors were 130 kilovolts, peak; 0.25 millimeter brass filtration, and 35 centimeter target skin distance, 5 milliamperes.

Twelve days after this treatment was finished, a 6 centimeter plastic applicator containing 104 millicuries of radon was inserted into the cervix for a dose of 3600 millicuries hours. The filtration was 0.5 millimeter platinum plus the wall thickness (1 mm.) of the plastic applicator. Unfortunately, this was not sufficient to control the cancer, for 2 months after the insertion of the radium persistence or recurrence was noted and confirmed by biopsy.

On October 22, 1943, a "stem and base" radium applicator was applied for 1000 millicuries hours, all the radon being in the base. Also, a single capsule was packed into left vault for 750 millicuries hours.

In spite of this treatment, a biopsy on January 3, 1944, showed active cancer. The cervix was still somewhat movable and the parametria were still not widely invaded with carcinoma. On February 4, 1944, a radical Wertheim hysterectomy was done. Operation was rendered difficult by the edema and fibrosis in the bases of both broad ligaments and between the trigone and vagina. Great care was taken to cause as little trauma as possible to the base of the bladder.

Postoperatively, a pack of zinc peroxide was placed daily against the suture line closing the vagina. In spite of this care, the upper vagina parted and a large cavity lined with necrotic tissue appeared in the area previously occupied by the uterus. The cavity slowly cleaned up and decreased in size, but the base of the bladder remained white. A small rectovaginal fistula appeared and then healed spontaneously. Two months after the radical hysterectomy, the white area in the bladder trigone separated, and the patient developed a large vesicovaginal fistula. It was so large that the index finger could be introduced with ease into the bladder through it.

The fistula was observed at frequent intervals from then on and various plans devised to try to diminish the leakage. A rubber condom was packed with cotton and inserted daily by the patient to try to stop the leak mechanically. This did not help. A contraceptive pessary was fitted to try to occlude the opening, again without improvement.

Thirteen months after the radical hysterectomy and 11 months after development of the vesicovaginal fistula, after three biopsies from the edge of the fistula had shown no carcinoma, the above described operation was carried out on March 1, 1945. The patient was kept flat on her abdomen in bed for 2 weeks, then gradually allowed to resume normal activities. A little urine leaked from the vagina postoperatively on one or two occasions when the suprapubic tube was kinked or plugged.

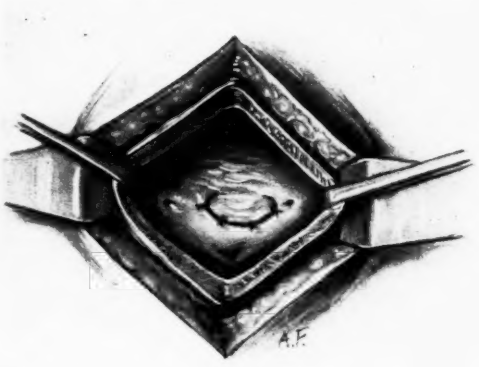


Fig. 6. Cystotomy view showing fistula edges sutured to patch.

She was discharged from the hospital 3 weeks after operation and has remained dry and free of any evidence of cancer since (8 months). Urinary control is normal. The result of the operation was a matter of intense joy and satisfaction to the patient. Repeated cystoscopic examinations clearly showed the patch of vaginal mucosa and on two occasions, thin, friable, white concretions were seen on its surface and scraped away with biopsy rongeurs.

The patient has had repeated sexual intercourse since her operation and, in spite of the shortening of the vagina which measures little more than 5 centimeters in length, reports satisfaction both to herself and husband after some adjustment.

Intravenous pyelograms made before the radical hysterectomy showed no hydronephrosis. After operation, they showed considerable hydronephrosis, most marked on the right side. This gradually diminished over the next month. Unfortunately no pyelogram was made immediately before the plastic closure of the fistula, but a recent intravenous pyelogram 8 months after this operation shows normal kidney function and no dilatation of the ureters.

CASE 2. Mrs. E. B. No. 52286. This 31 year old patient first entered Memorial Hospital on September 17, 1936, complaining of a foul-smelling, watery vaginal discharge first noticed 6 months previously during her third pregnancy. Examination revealed a large fungating carcinoma of the cervix, graded II on biopsy. It did not extend into the parametria and was classified as League of Nations stage I.

She was treated with external roentgen therapy to six 10 by 14 centimeters pelvic ports from September 21, 1936, to October 10, 1936, each port receiving first 100 r, then 150 r, 200 r, 250 r, 300 r and 350 r, for 1350 r per port. The factors were 200 kilovolt peak, 0.5 millimeter copper filter, 70 centimeter target skin distance, and 30 milliamperes. On October 26,

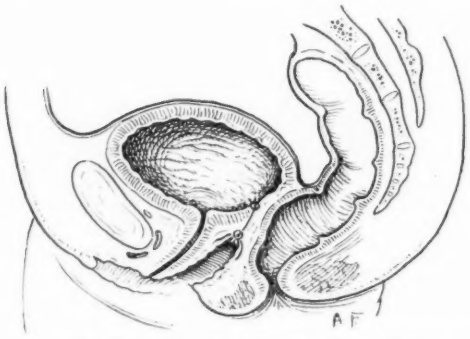


Fig. 7. Sagittal section showing end-result. (Cystotomy tube not illustrated.)

radium in a vaginal applicator (bomb) was placed against the cervix for 1500 millicuries hours. The next day a radium tandem was inserted into the cervical canal for 3000 millicuries hours. The filtration of both of these applicators was the equivalent of 0.5 millimeter of platinum.

On subsequent follow-up visits, it was noted that fluid accumulated inside the uterine cavity which gradually became purulent and foul. Dilatation of the cervix failed to provide adequate drainage and she became chronically ill by the prolonged sepsis.

Finally, as a palliative procedure on February 27, 1937, 4 months after radium treatment, a supracervical hysterectomy was performed, the dilated fundus which by then was a very foul sac of pus, being removed. During the operation, an attempt was made to dissect the base of the bladder off the cervix but this was abandoned because of the edema and fibrosis encountered. Most of the cervix was left *in situ*, a cigarette drain being passed down through its center into the vagina. No cancer was found in the operative specimen.

Postoperatively, a large abscess formed in the posterior cul-de-sac which began to discharge through the cervix a month after operation.

In May, 1937, she was hospitalized elsewhere because of acute abdominal pain, dysuria, and gross hematuria. While there, she had an acute vaginal hemorrhage and developed both rectovaginal and vesicovaginal fistulas. From then on, her general condition began to improve greatly so that in November, 1937, it was noted she looked well and had no complaint save for constant leakage of urine.

She was seen at frequent intervals in the follow-up clinic without developing any sign of recurrence of the cancer. Save for occasional bouts of cystitis, with some bleeding at times, she remained well. Frequent consultations were held as to the possibility of closing the fistulas, but it was generally agreed that any procedure toward this end was not feasible.

Finally in September, 1945, 8 years after the fistulas developed and after we had seen the success which attended the operative treatment of our first case, she was admitted again with the hope of performing a similar procedure.

Examination showed as in the first case a fistula on the anterior wall of the vagina at its apex through which the tip of the index finger could be inserted into the bladder. Introduction of methylene blue into the rectum showed it to pour out through the same opening. A barium enema done under fluoroscopic guidance with a thin barium solution showed this fistulous opening communicating with the mid-sigmoid. Intravenous pyelograms demonstrated a left hydronephrosis and hydroureter.

On September 13, 1945, the patient was operated upon as here described. Two observations should be made on this procedure; first, that it was necessary to open the abdomen and disconnect the sigmoid from the base of the bladder. The fistulous tract was turned in and closed by three layers of sutures in the wall of the bowel. The bladder defect could not be so treated because of the extensive fibrosis and consequently it was closed with interrupted sutures placed on the posterior side (i.e. in the cul-de-sac). The cervix was not seen.

The second point of note was that there was hydroureter of the left ureter which emptied through a tiny opening into the left lateral wall of the fistula. This opening could not be dilated sufficiently to allow the introduction of a fine probe or of a ureteral catheter and consequently only the right ureter was catheterized. An attempt was made to dissect the left ureter free and reimplant it in the bladder. There was such marked radiation fibrosis of the ureter all along its course in the pelvis that it could not be separated safely, and the attempt was abandoned.

The patient was kept on her abdomen for 8 days after operation. When she was allowed to turn on her back after that time, urine began to leak through the vagina. Finally with the help of constant gentle suction on the suprapubic cystotomy tube, she was kept dry and healed solidly. A brief febrile episode, due to left pyelonephritis, cleared with penicillin therapy. She was discharged from the hospital on the thirty-eighth postoperative day.

Since then she has remained well and completely dry with normal control of urine. The vagina is 6 centimeters deep and completely healed. Cystoscopic examination shows the patch to be covered by a small amount of white, easily removed exudate. Intravenous pyelogram shows no change compared with the examination before operation. The patient has had sexual intercourse since operation.

CASE 3. M. C. No. 72338. This 45 year old patient first entered Memorial Hospital on November 29, 1943, with cancer of the cervix classified as League of Nations, stage III, because it extended in the left parametrium to the pelvic wall with fixation on that side.

She had been treated at another hospital on March 21, 1943, with 2000 millicuries hours of radium in capsules inserted into the cervical canal. This was repeated on May 9. In October, vaginal bleeding recurred and at the same hospital on October 2

2000 millicuries hours of radium was administered for the third time.

Since a biopsy on admission to Memorial Hospital showed epidermoid carcinoma, grade II, roentgen therapy was begun on December 3 and continued until January 4, during which time each of six 14 by 11 centimeters pelvic ports received 250 r times 8, or 2000 r. The factors were 200 kilovolt peak, 0.5 millimeter copper filter, 70 centimeter target skin distance, and 30 milliamperes. On January 13, 1944, a vaginal bomb was placed against the cervix for 1500 millicuries hours. On January 14, a radium tandem was inserted into the cervical canal for 3000 millicuries hours.

Three months later it was noted that the cervix had been replaced by a large crater filled with foul-smelling slough.

On January 31, 1945, a year after her last radium treatment, a large vesicovaginal fistula at the upper end of the vagina was seen but all evidence of cancer had disappeared save for thickening and scarring in the left parametrium. She complained of complete urinary incontinence. Biopsies from the edge of the fistula showed no evidence of cancer.

Consequently, on September 27, 1945, a year and 9 months after the last radium treatment, the fistula was repaired by the technique already described. The left ureter, as in the other 2 cases, was found opening into the margin of the defect, but no evidence of hydronephrosis or hydroureter could be demonstrated by intravenous pyelography preoperatively. The operation was somewhat easier than those in the other 2 cases because the tissues of the bladder and vagina were more elastic and had a better circulation. The uterus was still present. A hysterectomy had not preceded the fistula repair but the uterine canal and cervix had been completely destroyed by the radium she had received.

Postoperative convalescence was uneventful and no urine came from the vagina at any time. She was allowed out of bed on the fifteenth postoperative day. The suprapubic catheter was removed on the seventeenth day. She was discharged dry, with complete urinary control on the twenty-third day after operation.

A month and a half later, cystoscopy showed the patch of vaginal mucosa in the base of the bladder to be clean, pale and not inflamed. The vagina was about 4 centimeters in length and the patient reported that she had had sexual relations satisfactorily without discomfort. Intravenous pyelograms showed that both kidneys excreted the dye at 5 minutes. There was no evidence of obstruction in either ureter. There were still some thickening and scarring felt by rectum in the base of the left broad ligament, but the clinical opinion was that this represented radiation fibrosis and not recurrent cancer.

DISCUSSION

This method of closure was devised without reference to published articles on the subject but, as commonly happens, we now find that many of its individual features have been used and described before. However, the plan of attack as a whole seems original. Such time-honored principles as lack of tension, preservation of blood supply, separated suture lines and a wide area of coapted raw surfaces are included. The operation of colpocleisis, partial or total, is old but is at times still advised (1, 2, 3, 4, 5, 6). It was devised first by Gustav Simon, of Darmstadt, in 1855 and later by Dr. Nathan Bozeman, of New York. Simon's operation of colpocleisis left the uterus emptying into the bladder and also left a dependent diverticulum in the bladder floor. Cystitis and calculus formation were common sequelae. Latzko improved this operation and incidence of these sequelae are less in his hands.

Our operation does not leave the uterus emptying into the bladder at all since the uterus has been removed or destroyed by radium, nor does a diverticulum result. Thus far no calculi have formed, the patients have not been troubled with cystitis symptoms after the immediate postoperative period, and repeated cystoscopic check-ups have found a steady diminution in the inflammatory re-

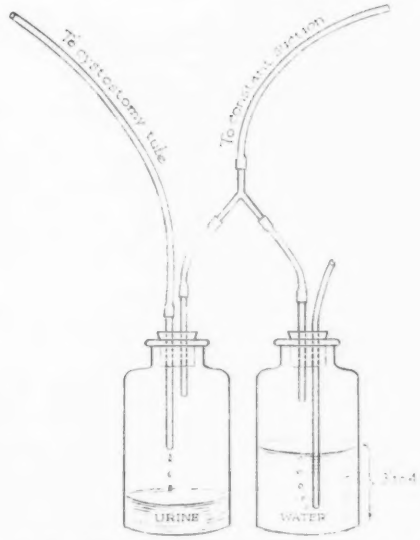


Fig. 8. Diagram of low pressure, "bubble," suction drainage.

action about the patch site. Complete obliteration of the vagina may be necessary rarely but has the objection of excluding normal sexual activity—not uncommonly an important item with these patients. The partial obliteration resulting from our procedure has in each instance left a vagina of 4 to 6 centimeters in length and all patients have had sexual relations since operation, though some adjustment was necessary.

The idea of using a patch of tissue from the posterior vaginal wall is also by no means new. Trendelenburg, in 1890, described a two stage operation on the pedicle graft principle to transfer a patch from the posterior vaginal wall to cover the fistula in the anterior wall. J. R. Miller in the discussion of another paper mentioned a case with a "blowout patch" of vaginal mucous membrane closing the fistula. This operation by Miller was very nearly like ours but apparently the suprapubic approach was not used. Witzel described the use of a patch of mucosa from the posterior vaginal wall sewed into the fistulous opening but did not accompany this by partial colpocleisis. The suprapubic approach has been described and perfected many times since Trendelenburg first advocated it in 1890. Catheterization of the ureters during operation is, of course, not original. In this connection, it might be well to remember that the only patient operated upon in London by the famous J. Marion Sims died because the ureters were included in the sutures (8). Various methods, including cystostomy, have been used to provide adequate drainage postoperatively. The indwelling urethral catheter rests on the newly repaired area and always sets up some urethral inflammation, but a well placed and cared for cystostomy tube does neither of these. Many plans for constant emptying of the bladder have been devised but the prone position and the low pressure, "bubble" suction seem the most efficient to us. The continuous prone position becomes a hardship to the patient and may allow the suprapubic tube to kink without the nurse's knowledge. However, it is simple and to the point. Low pressure suction is more comfortable but the apparatus requires constant attention and does not prevent slight leakage through the repaired area, particularly for the most important first few postoperative days.

SUMMARY

Repair of vesicovaginal fistulas in heavily irradiated tissues is peculiarly difficult because the local blood supply is precarious, the tissues are inelastic and fixed, and the tissues are so fibrotic as to make dissection, particularly of flaps, quite difficult. Also the frequent intimate association of the ureteral orifices adds to the problem greatly.

The plan described is to be used only where residual cancer is ruled out, where the uterus and cervix are removed, or clearly obliterated, and where the urinary status after fistula closure would be expected to be satisfactory (especially good sphincter control). Sexual activity after operation is possible.

The operation is a combined transvesical and vaginal approach which permits complete safety to the ureteral orifices in or near the opening; a two suture line closure with these lines separated by at least a 2 centimeter adhering area of raw surfaces; a minimum damage to blood supply; closure without tension; relatively simple and easy dissection; and adequate bladder drainage during the postoperative period without a foreign body irritating the newly repaired area.

Postoperative care is directed toward continuous gentle bladder drainage and cleanliness of the wounds.

Only 3 cases are reported but the successful result in each, considering the unfavorable preoperative condition, seems to indicate the value of the method.

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MANDIBULAR TUMORS

A Clinical, Roentgenographic, and Histopathologic Study

LOUIS T. BYARS, M.D., F.A.C.S., St. Louis, Missouri, and BERNARD G. SARNAT, M.D., Chicago, Illinois

THE diagnosis of ameloblastoma (adamantinoma) of the mandible has been made frequently by use of only the roentgenogram. The multilocular appearance in the roentgenogram is supposed by some to be characteristic of the ameloblastomas. It is the purpose of this report to demonstrate that (1) many jaw tumors can produce a similar roentgenographic picture, and (2) ameloblastomas have not a constant characteristic roentgenographic picture. Consequently the roentgenogram alone cannot be depended upon for a diagnosis of ameloblastoma or of any other type of jaw tumor.

CASE REPORTS

The following series of 12 case reports including roentgenograms and photomicrographs has been carefully selected principally from our office and hospital files on mandibular tumors. The pertinent findings are summarized in Table I. The series has been divided into two groups.

I. Ameloblastomas with varying roentgenographic findings.
   - A. Roentgenogram "typical" of ameloblastoma.
   - B. Roentgenogram similar to that of a dentigerous cyst.
   - C. Roentgenogram similar to that of a retained root fragment and cyst.
   - D. Roentgenogram similar to that of an invasive tumor of bone.

II. Benign and malignant tumors (other than the ameloblastoma) which appear multilocular on the roentgenogram.
   - A. Multiple follicular cyst.
   - B. Giant cell tumor (local).
   - C. Giant cell tumor (general). Hyperparathyroidism.
   - D. Fibroma.
   - E. Fibrosarcoma.
   - F. Osteogenic sarcoma.
   - G. Metastatic carcinoma from the breast.
   - H. Metastatic carcinoma from the thyroid.

From the Department of Surgery, Division of Plastic Surgery Washington University Medical School.

Ameloblastomas with Varying Roentgenographic Findings

Roentgenogram "typical" of ameloblastoma. C.E.S., white male, aged 71 years, was first seen on October 11, 1940. Several years before, the patient noticed the left side of his jaw was enlarged. Physical examination revealed a hard nonmovable mass which extended from one centimeter below the zygomatic process to the lower border of the ramus. Intraoral examination revealed a fistula in the region of the lower left third molar. On October 12, 1940, through an intraoral incision a large cyst was removed from the left mandible at the angle. Iodoform and balsam of Peru pack was inserted. The tissue on cut section was white, fibrous, rather firm, and not characteristic. The microscopic diagnosis was ameloblastoma (Fig. 1 a).

The patient was next seen on December 2, 1941, and complained that 3 months before the jaw began to swell at the left angle again. Some pain which was not very severe was present. The patient was operated upon December 3, 1941, and because the ameloblastoma had "recurred," causing a pathological fracture of the mandible, and because the tumor was no longer contained within the mandible but invading the surrounding tissue, cautery destruction of the growth was done.

Roentgenogram similar to that of a dentigerous cyst. B.J.B., white female, aged 17 years, was first seen on February 12, 1945. Patient stated that she had a "gum boil" at the back of the left jaw for the previous 6 weeks. Physical examination revealed a soft tissue mass in the left retromolar area which was 0.5 centimeter in diameter. The mass was neither tender nor movable. There was a moderate expansion of the body of the mandible in this area. On March 8, 1945, an incision was made in the retromolar area, the mucoperiosteum was reflected laterally and the lingual nerve was preserved. An entrance was gained to the cyst cavity by removal of the thin plate of bone. There was considerable solid material which was removed completely from the cyst wall. The cavity was packed with iodoform gauze. Histopathologic diagnosis was ameloblastoma (Fig. 1 b).

Roentgenogram similar to that of a retained root fragment and cyst. F.M.A., white male, aged 40 years, was first seen March 29, 1938. Patient first noticed a lump in the right mandible about 1 centimeter in diameter, 6 weeks before while shaving. There was no pain. There had been drainage into the mouth from the region of the mass for 1 week.

TABLE I.—CHARACTERISTICS OF MANDIBULAR TUMORS WHICH APPEAR MULTILOCULAR ON THE ROENTGENOGRAM

Histopathologic diagnosis of various cases	Age when seen years	Clinical history	Clinical findings	Location in mandible	Edentulous areas	Miscellaneous
I A Ameloblastoma See Fig. 1 a	71	Several years ago left side of mandible enlarged. Discharge from molar area 6 months ago. Reoperated upon 14 months later	Hard, nonmovable mass extending from 1 cm. below zygoma to lower border of ramus	Angle and ramus	Complete mandible	Pathologic fracture—subsequently
I B Ameloblastoma See Fig. 1 b	17	"Gum boil" behind last tooth of mandible 6 weeks	0.5 cm. mass, retromolar area, moderate expansion of mandible	Angle and most of ramus	None	
I C Ameloblastoma-odontome See Figs. 1 c & e	40	1 cm. lump back part of mandible noticed 6 weeks previously while shaving	Firm, fixed, nontender, 5 cm. mass extending from mental foramen to angle	Molar area	Involved area	
II A Multiple follicular cyst See Fig. 2	45	Pain in jaw 8 months. Lower teeth extracted 7 months ago; swelling of jaw and discharge 2 weeks	Moderate enlargement of mandible from angle to cuspid area. Draining sinus molar left area	Molar area, angle, and ramus	Complete mandible	Bilateral involvement of mandible
II B Giant cell tumor (local) See Fig. 3	13	Painless, progressive swelling both sides of mandible for 6 years	Both rami of mandible enlarged and irregular	Everything posterior to bicuspid area except condyle	Involved area	Blood serum calcium and phosphorus within normal limits. Bilateral involvement of mandible
II C Giant cell tumor (hyperparathyroidism) See Fig. 4	40	Painful jaw 13 years; all teeth extracted 4 years ago. Four weeks ago mandible began to swell	Smooth, sharply outlined tumor which extended halfway up anterior border of ramus. 1 cm. mass in maxilla near ala of nose. 3 x 1 cm. mass region of thyroid gland	Angle	Complete mandible	*Preoperative* Bl.S.ca., 14.6 mgm. % Bl.S.P., 2.4 mgm. % *Postoperative* Bl.S.ca. 9.2 mgm. % Bl.S.P. 5.1 mgm. %
II D Fibroma See Fig. 5	15	Swelling of jaw, 4 months, sharp shooting pains to ear and some disability in use of jaw. Dentist stated trouble caused by erupting wisdom tooth	Firm, fixed, nontender mass in parotid region and extended to angle of jaw	Angle and ramus	None	
II E Fibrosarcoma See Fig. 6	4	Intermittent toothache for 8 weeks; rapid swelling of face and mandible, 6 weeks. Dentist and otolaryngologist found nothing wrong. Sulfanilamide prescribed	Large, hard mass which extended from lower border of mandible to upper border of ear	Molar area and everything posterior	Involved area	
II F Osteogenic sarcoma See Fig. 7	20	Swelling of mandible, 5 months. Diagnosis of impacted wisdom tooth which was extracted. Wound did not heal	Diffuse, firm swelling at angle of jaw. Surrounding tissues indurated. Unable to open mouth	Molar area, angle and ramus	None	
II G Metastatic carcinoma from breast See Fig. 8	57	Numbness and tingling of lower lip and lump in mandible 6 months. Molars in area extracted and 8 deep x-ray therapy treatments with no relief. Diagnosis of carcinoma of breast 1½ years ago	Nontender, round, hard mass, 1.5 cm. in diameter in about molar region	Molar area	Involved area	
II H Metastatic carcinoma from thyroid See Fig. 9	55	Dull pain in mandible 5 weeks	Resilient mass, lingual premolar region of mandible. Stony hard diffuse enlargement of right lobe of thyroid gland	Bicuspid area	Complete mandible	Tumor also metastasized to right iliac crest

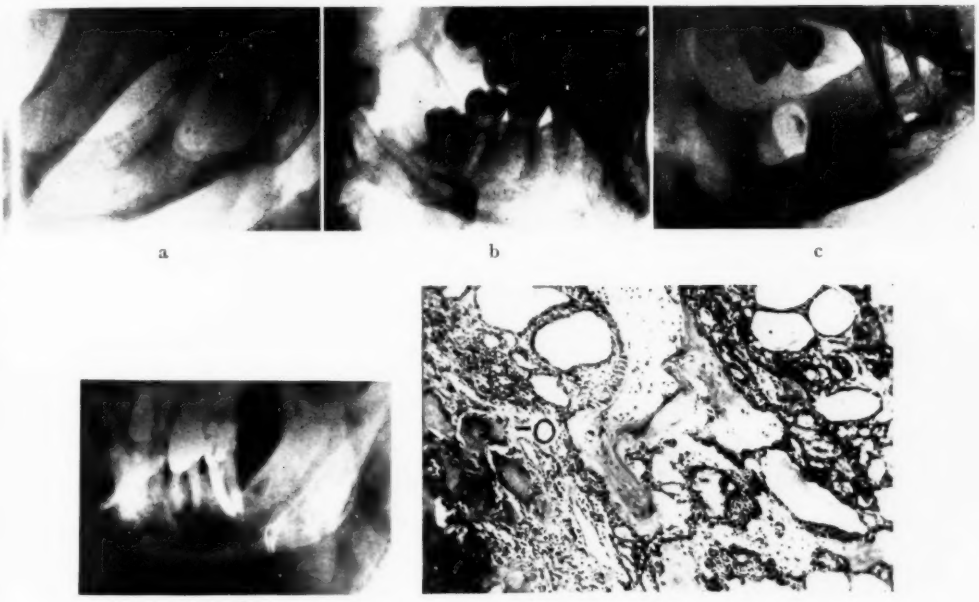


Fig. 1. Roentgenograms illustrating the various patterns which the ameloblastoma may assume: a, "typical" of an ameloblastoma; b, similar to that of a dentigerous cyst; c, similar to that of a retained root fragment and cyst (a and c from Byars and Sarnat, *Surg. Gyn. Obst.*, 1945, 81: 575); d, ameloblastoma with infiltrating characteristics (courtesy of C. V. Mosby Co., St. Louis, Mo. From Thoma, *Oral Pathology*, Fig. 937 A, 2nd ed., 1944); e, photomicrograph obtained from specimen in Case I C. Note the columnar cells arranged in a palisade formation. In the center of these areas there appears to be a clear cytoplasm, the margins of which cannot be determined because of the fine reticulum. There is a moderate amount of dense connective tissue stroma between the groups of tumor cells. Note areas of osteodentin, *O*. Diagnosis: ameloblastoma —odontome (Fig. 1c).

Physical examination revealed no teeth in the lower right jaw and a firmly fixed nontender mass about 5 centimeters in diameter, extending from about the mental foramen to the angle. On March 31, 1938, patient had a resection of the mandible. Surgical specimen consisted of a round, firm tumor attached to a portion of the mandible. When cut, there was a very distinctly gritty sensation to the knife. The cut surface presented a very cellular appearance. The histopathologic diagnosis was ameloblastoma and odontoma (Figs. 1 c and e).

Patient was seen in April of 1940 and there was no evidence of recurrence. In August, 1944, the patient wrote that jaw has never given him any trouble.

Roentgenogram similar to that of an invasive tumor of bone. Figure 1 d is an illustration of an ameloblastoma similar to that of an invasive tumor of bone.

Benign and Malignant Tumors (Other Than the Ameloblastoma) Which Appear Multilocular on the Roentgenogram

Multiple follicular cyst. J.W.J., white male, aged 45 years, was first seen November 27, 1942. Patient complained of pain in the lower jaw since about March, 1942. In April of 1942 he had all of his lower teeth extracted. There had been a foul taste in the mouth for the previous 6 months. In early November he noticed a swelling in the left lower jaw and since that time there had been a discharge of grayish material. Physical examination revealed a fistula in the lower left molar area. On November 28, 1942, through an intraoral approach the cysts of the mandible were excised bilaterally. The cyst wall was white, thin, but firm. The inner wall of the cyst was glistening and the cyst contained fine brown, friable material. The histopathologic diagnosis was multiple follicular cyst (Fig. 2).

Giant cell tumor (local). B.A.L., white female, aged 13 years, was first seen on April 15, 1942. About 6 years before patient noticed swelling of both sides of the face unaccompanied by pain. From 1936 to 1938 patient had 8 operations on the mandible. There was no similar condition in any other member of the family. Examination revealed that both rami of the mandible were enlarged and irregular, but normal in dimension in the long axis. On July 8, 1942, there were the following laboratory findings:

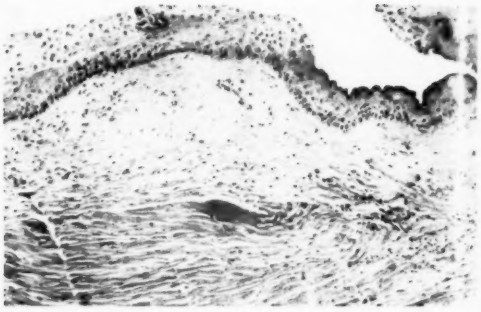
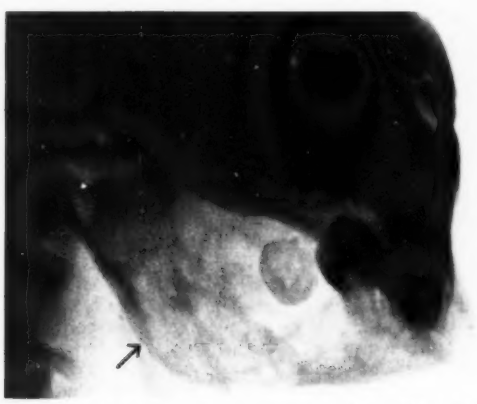


Fig. 2. a, left, Lateral roentgenogram of mandible. The histopathologic diagnosis is multiple follicular cyst (Fig. 2b). b, Photomicrograph of specimen obtained from Case II A. Note cyst wall, the lining of which is made up of stratified squamous epithelium. Diagnosis: Multiple follicular cyst (Fig. 2a). ×70.

blood serum calcium, 11.1 milligrams per cent; blood serum phosphorus, 4.9 milligrams per cent; blood serum phosphatase, 9.4 Bodansky units.

On July 9, 1942, an incision was made on the left side of the neck in the fold from the side of the thyroid cartilage to the base of the ear. This flap was dissected upward exposing the right side of the mandible on the outer plate of which was a hard, raised, bluish discoloration. The outer plate was removed by chisel and a tumor mass exposed, which ran throughout the anterior two-thirds of the mandible on its right side. The tumor was removed by curettement and chisel, but due to its numerous ramifications in the bone, it was highly improbable that all the cells were removed completely. The tumor was fragmented, fairly firm yellowish-gray. The cavity in the mandible was packed with iodoform gauze led through the soft tissues to the exterior. The histopathologic diagnosis was giant cell tumor (Fig. 3). Roentgenograms taken periodically have shown regression of the tumor area. There was no recurrence up to March, 1945.

Giant cell tumor (general), hyperparathyroidism. L.C.C., white female, aged 40 years, was first seen on March 26, 1941. Patient stated that she had an abdominal operation in 1928 and since that time the right side of her jaw had been sore. Two years later two teeth were extracted and the jaw condition became worse. About this time patient began to have attacks of vomiting which continued for 11 months when she was operated upon for a floating kidney without any subsequent relief. About 2 years before, patient experienced severe pain in jaw and thought something broke. Because of weakness she was suspected of having tuberculosis. Four weeks previously the right side of the jaw began to swell. Examination revealed a tumor of the right mandible which was smooth and sharply outlined and went



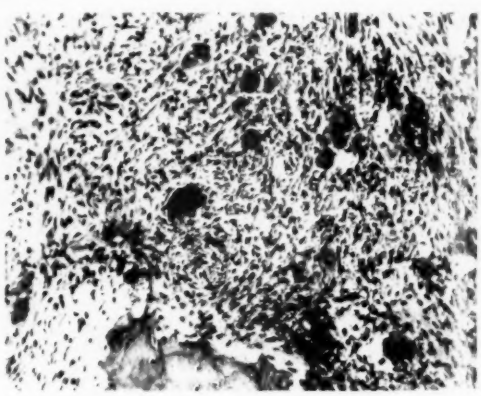
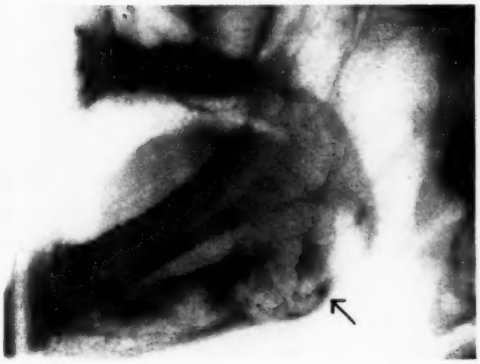


Fig. 3. a, left, Lateral roentgenogram of mandible. The histopathologic diagnosis is giant cell tumor (Fig. 3 b). b, Photomicrograph of specimen obtained from Case II B. Note bone the margins of which are irregular and are being destroyed, and also bone formation. In addition note t dense collection of fibroblastic cells in which there are ma multinucleated giant cells. Diagnosis: giant cell tumor mandible (Fig. 3 a). ×70.



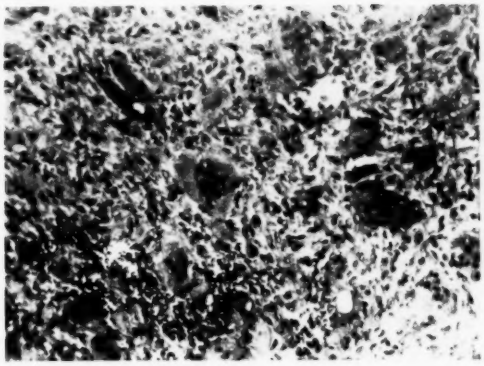


Fig. 4. a, left, Lateral roentgenogram of the mandible. The histopathologic diagnosis is giant cell tumor. The patient had a parathyroid adenoma (Fig. 4 b). b, Photomicrograph of specimen obtained from Case II C. Note the fibrous connective tissue which contains an enormous number of multinucleated giant cells. Diagnosis: giant cell tumor of mandible (Fig. 4 a). (Also see Table I and contrast with Case II B). ×125.

halfway up on the anterior border of the ramus. There was a distinct swelling 1 centimeter wide at the level of the nose near the ala. There was a tender 3 by 1 centimeter node on the right side in the region of the thyroid gland. At laboratory examination the following findings were revealed: blood serum calcium, 14.6 milligrams per cent; blood serum phosphorus, 2.4 milligrams per cent; blood serum phosphatase, 11.8 Bodansky units.

On March 27, 1941, tumors were removed from both upper and lower jaws on the right side. Following this a parathyroid tumor was removed deep to the lower pole of the thyroid on the right. The jaw material consisted of several small pieces of irregularly shaped brownish friable tissue. The histopathologic diagnosis was giant cell tumor (Fig. 4). Laboratory findings on the seventh postoperative day revealed the following: blood serum calcium, 9.2 milligrams per cent; blood serum phosphorus, 5.1 milligrams per cent. On October 9, 1944, patient stated that she felt perfectly all right.

Fibroma. L.C.H., white female, aged 15 years, was first seen on December 1, 1944. Patient complained of swelling of the right jaw since August, 1944. At that time a dentist said that a wisdom tooth was erupting. The growth had increased in size somewhat since and there had been sharp shooting pains in the right ear, in addition to some disability in the use of the jaw. Two weeks before a physician took a roentgenogram and told her the mass was attached to the bone. Physical examination revealed a visible lump in the right parotid region. It was firm, not movable, and not tender, and extended to the angle of the jaw. There was some limitation of movement of the jaw. The teeth were in good condition.

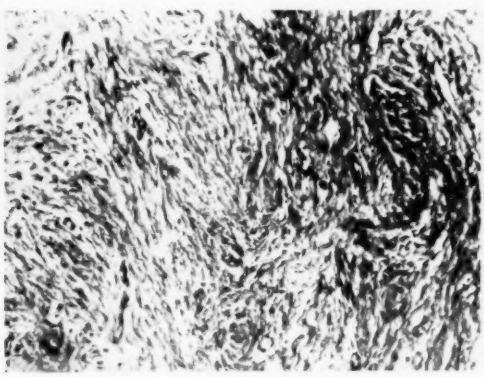
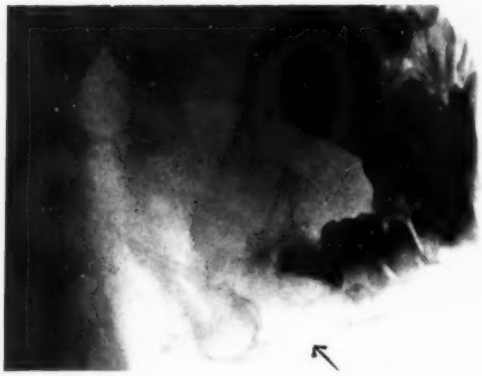


Fig. 5. a, left, Lateral roentgenogram of the mandible. The histopathologic diagnosis is fibroma (Fig. 5 b). b, Photomicrograph of specimen obtained from Case II D. The tumor is an acellular collagenous fibroma of bone the cell origin of which is indeterminate. Diagnosis: fibroma (Fig. 5a). ×125.



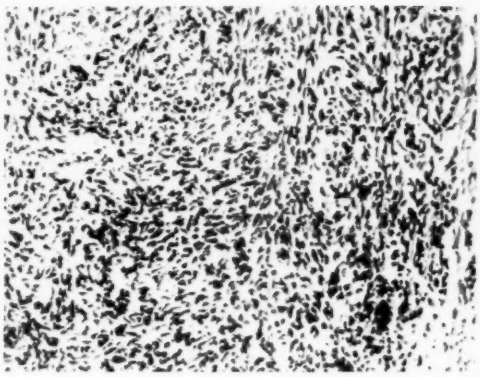
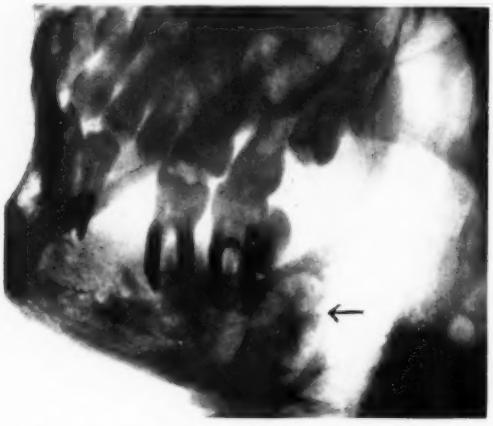


Fig. 6. a, left, Lateral roentgenogram of mandible. The histopathologic diagnosis is fibrosarcoma (Fig. 6 b). b, Photomicrograph of specimen from Case II E. The tumor is extremely cellular. The individual cells are spindle shaped to rounded, the nuclei are variable in size, shape, and staining reaction; many are hyperchromatic; numerous mitotic figures seen. This is a rapidly growing neoplasm of fibroblastic origin. Diagnosis: fibrosarcoma (Fig. 6 a). ×125.

On December 2, 1944, an incision was made from below the lobe of the right ear forward under the mandible to below the lateral incisor region. Skin, subcutaneous tissue, platysma, lower pole of the parotid and tissue superficial to submaxillary salivary gland were all turned upward to expose the angle and body of the mandible. The masseter muscle was dissected free from the ramus, exposing the entire ramus and angle which were involved by the tumor. The mandible was sectioned at the last molar tooth. The ramus was disarticulated and removed. Another half inch of bone was removed from the forward fragment because it was questionable whether the tumor had been encroached upon at the point of section. The jaws were wired in occlusion.

The surgical specimen consisted of the right ramus of the mandible which was surrounded and permeated by a firm, resilient, nonfriable white tumor mass. The specimen cut with increased resistance and showed a thin white capsule which completely surrounded the tumor mass. The cut surface of the mass was yellow with streaks of white tissue running through it. It showed some evidence of hemorrhage but no cystic changes grossly. The tumor was growing on both sides of the mandible, which was thin and showed evidence of bone destruction. The histopathologic diagnosis was fibroma (Fig. 5).



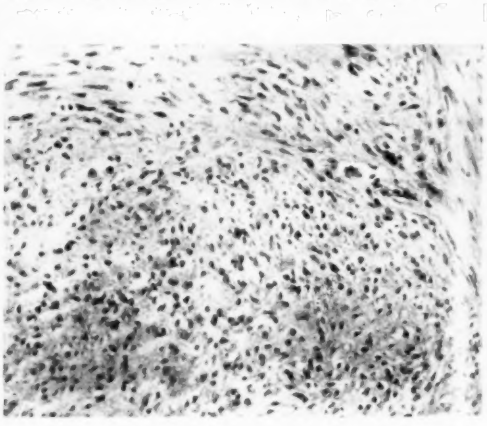
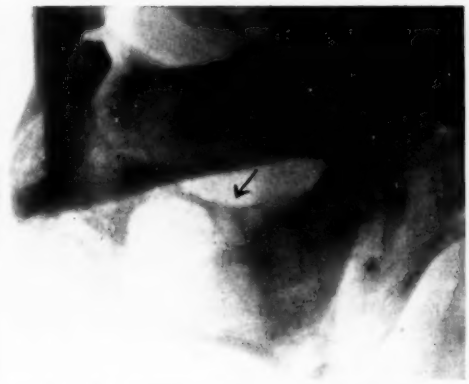


Fig. 7. a, left, Lateral roentgenogram of mandible. The histopathologic diagnosis is osteogenic sarcoma (Fig. 7 b). b, Photomicrograph of specimen obtained from Case II F. Note thick layer of fibrous tissue which is growing without any plan. The cell outlines are not sharp. The nuclei are for the most part elongated and vary in size, shape, a staining reaction. An occasional mitotic figure is seen. other areas abnormal bone formation is seen. Diagnos osteogenic sarcoma from membranous bone (Fig. 7 ×125.



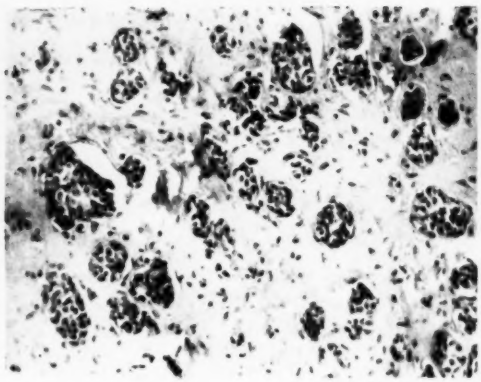
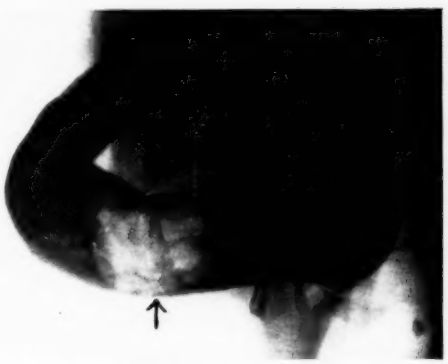


Fig. 8. a, left, Lateral roentgenogram of the mandible. The histopathologic diagnosis is metastatic carcinoma from the breast (Figs. 8 b and 1 d). b, Photomicrograph of specimen obtained from Case II G. Note islands of malignant undifferentiated epithelial cells. Diagnosis: carcinoma of the mandible (metastatic from the breast) (Fig. 8 a). ×125.

Fibrosarcoma. H.F.G., white male, aged 4 years, was first seen on January 4, 1945. About 8 weeks before the patient suddenly began to complain of intermittent toothache in the left mandible. Patient was examined by a dentist who found nothing wrong. The patient was examined by an otolaryngologist who likewise found nothing wrong and prescribed sulfanilamide. About 6 weeks previously a mass about the size of a grape was noticed in the left jaw. This continued to grow until at the present time it involved a considerable portion of the face. Extraoral examination revealed a large, hard, moderately tender mass which extended from below the lower border of the posterior part of the mandible up to the superior border of the ear. The anterior portion of the ear was pushed outward with the mass. Intraoral examination revealed a mass arising from the mandible behind the last molar. The mass pushed the left tonsillar area over to the midline of the pharynx. On January 6, 1945, biopsy was made on the jaw tumor. The histopathologic diagnosis was fibrosarcoma (Fig. 6).

Osteogenic sarcoma. Y.M.B., white female, aged 20 years, was seen on October 16, 1940. In July, 1940, the patient stated that her jaw on the left side began to swell. Patient went to a physician who took roentgenograms and said there was an impacted wisdom tooth. Physical examination revealed a diffuse swelling at the left angle of the jaw, firm and sensitive to pressure. The surrounding tissues were indurated. Patient was unable to open her mouth.

On October 17, 1940, an incision was made on the left side of the neck and the tissues elevated from the mandible. It was found that the entire half of the



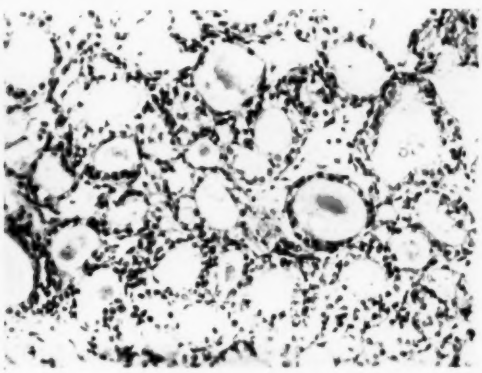


Fig. 9. a, left, Lateral roentgenogram of mandible. The histopathologic diagnosis is metastatic carcinoma from the thyroid (Fig. 9 b). b, Photomicrograph of specimen obtained from Case II H. The thyroid glandular tissue is hyperplastic. The cells as a whole are well differentiated. Abnormal mitotic figures are not observed. Diagnosis: carcinoma of mandible (metastatic from thyroid) (Fig. 9 a). ×125.

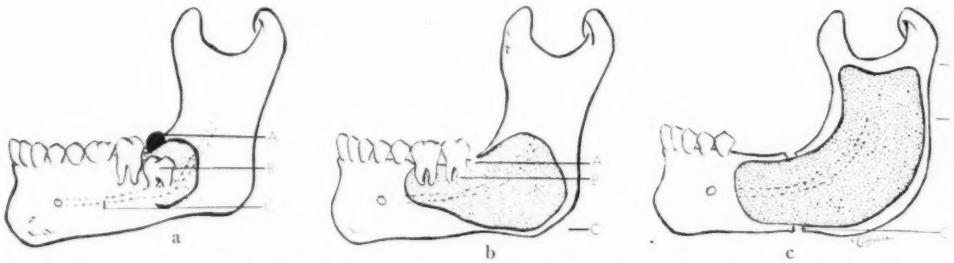


Fig. 10. Common errors made in diagnosis of jaw tumors. Presenting signs, symptoms, findings, and common misdiagnoses. a, Gum boil, granulation tissue, *A*; impacted molar, *B*; paresthesia and anesthesia of lip, pain in teeth and mandible, *C*. b, Draining sinus, *A*; loose teeth, pyorrhea, *B* (Pyorrhea is not the only cause for loose teeth); swelling of face, *C*. c, Pain in ear, *A*; limitation of movement of jaw, *B*; fracture, *C*.

mandible was involved with an invasive tumor. It was definitely malignant and too extensive to offer any hope of cure from a radical operation. The histopathologic diagnosis was osteogenic sarcoma (Fig. 7). Patient died on June 18, 1941.

Metastatic carcinoma from the breast. C.S.F., white female, aged 57 years, was first seen February 11, 1943. Patient complained of numbness and tingling of the lower lip since August, 1942. In addition at that time a lump was noticed in the right mandible. Patient went to a dentist who extracted the right lower molars, but there was no relief from the symptoms. She went to a physician who gave 8 deep x-ray therapy treatments. Patient had a left radical breast removal for carcinoma 1½ years previously and there had been no evidence of recurrence. Physical examination revealed a nontender, round, hard mass, 1.5 centimeters in diameter, in the right mandible at the molar region.

On February 12, 1943, in the region of the right molar, the buccal plate was removed exposing a hard tumor 3 by 2 by 2 centimeters which was removed and the bed cauterized with heat. The specimen was white, very firm and appeared to be fibrous tissue. Tissue was sent to surgical pathology for rapid frozen section. The histopathologic diagnosis was metastatic carcinoma from the breast (Fig. 8).

Metastatic carcinoma from the thyroid. E.L.W., white female, aged 55 years, was first seen on October 25, 1938. This patient complained of dull pain in the left mandible for 5 weeks. Her dentist took roentgenograms of the jaw and found destruction of bone. Patient stated that she had had a goiter for 25 years, but it had remained unchanged. Physical examination revealed that on the lingual surface of the left lower jaw in the premolar area there was a mass which extended down to the lower border of the jaw. It was palpated on the outside where it was quite painful. There was a stony hard diffuse enlargement of the right lobe of the thyroid gland.

On October 26, 1938, an opening was made into the jaw bone and a rather vascular type of tumor was removed. The microscopic report was metastatic carcinoma from the thyroid (Fig. 9). On November 2, 1938, the right lobe and the isthmus of the thyroid gland were removed and the microscopic report was adenocarcinoma of the thyroid. Patient was again seen on June 7, 1942, complaining of pain in the right iliac crest and difficulty in walking. Two series of x-ray therapy each consisting of 2400 roentgen units were given to this area. Patient was again seen on March 31, 1943, and she stated that she had pain in the left mandible since October, 1942, and during the last few months a lump had appeared. She had had no complaints in regard to the jaw since the last operation of 1938. The mass was excised by means of cautery and found to be metastatic thyroid tissue. The tumor of the ilium was also excised and this too was found to be adenocarcinoma of the thyroid. The patient was last seen in 1945 and no evidence of carcinoma was found.

DISCUSSION

Roentgenograms of the mandible. Entirely satisfactory roentgenograms of the mandible are usually difficult to obtain. The masseter and internal pterygoid muscles, the pharynx and other soft tissue structures interfere. In addition, superposition of the other side of the mandible, the maxilla, the vertebrae, and the thyroid bone confuse the picture. Comparison of preoperative roentgenograms of the mandible with roentgenograms of the resected tumor and mandible reveal striking differences (1). The latter, devoid of surrounding tissue, show remarkably sharp. This problem is partly answered clinically by use of the laminagram.

Classification of "cystic" lesions of the mandible. Any practical clinical classification of "cystic" lesions of the mandible should be all inclusive. Many errors are made in the clinical diagnosis of jaw tumors (Fig. 10). The histopathologic diagnosis is specific. The roentgenographic diagnosis, however, is non

specific and includes many tumors which are radiolucent but not truly cystic. Consequently, in the differential diagnosis the following should be considered on a roentgenographic basis.

TUMORS OF THE MANDIBLE

I. Tumors of dental origin.
  A. Follicular cyst (single and multiple).
  B. Dentigerous cyst.
  C. Ameloblastoma (preameloblastoma).
  D. Radicular cyst (or granuloma).
II. Tumors of nondental origin.
  A. Primary in mandible.
    1. Benign—
      a. Giant cell,
      b. Eosinophilic granuloma,
      c. Fibroma,
      d. Traumatic.
    2. Malignant—
      a. Carcinoma (local spread),
      b. Sarcoma (fibrosarcoma osteogenic sarcoma, Ewing's).
  B. Secondary in mandible.
    1. Metastatic sarcoma and carcinoma.
    2. Altered body metabolism—
      a. Hyperparathyroidism,
      b. Lipoid disturbances (Gaucher's, Christian Schuller, etc.)

To the surgeon and dentist this classification is more valuable than one developed on a strict pathological basis of truly cystic lesions. It is important for the dentist to realize that "cystic" lesions of the mandible can be other than dental in origin and that they may not be primary in the mandible, but metastatic. Consequently it behooves the dentist and dental surgeon to be fully cognizant of the variety of "cystic" lesions of the mandible and to make early provision for adequate treatment. By the same token the oral surgeon must be prepared at the time of operation to do either a relatively simple enucleation of a true cyst or a difficult radical resection of the mandible for a malignant tumor.

Roentgenographic and clinical characteristics of the ameloblastoma. The roentgenographic characteristics of the ameloblastoma are supposed to show multilocular radiolucent areas with a sharp smooth border. This is surrounded by a thin, narrow, radio-opaque zone. Smaller daughter areas connected with a larger radiolucent area have also been described as being characteristic. This description is probably better adapted to the cystic phase of the tumor. There is no reason why any other cystic tumor should not look the same. Even solid tumors show a striking similarity. One should also remember that the ameloblastoma may be either unilocular, entirely solid, or solid and cystic and consequently the roentgenographic picture may be far from the "normal" (Fig. 1).

The ameloblastoma is generally considered to be a benign tumor. Because local recurrence is frequent, it has been sometimes said to be malignant. Complete removal of the tumor is made more difficult because of daughter cysts. Consequently what is believed by some to be a local recurrence is actually an incomplete removal. Rarely, the ameloblastoma will undergo true malignant degeneration and metastasize.

Because the ameloblastoma is generally considered to be a benign tumor, and because the roentgenographic pictures may be similar to malignant lesions primarily or secondarily in the jaw, it is of paramount importance to make an early correct diagnosis.

SUMMARY AND CONCLUSIONS

Multilocular radiolucent areas in the roentgenograms of the mandible have been demonstrated for ameloblastoma, multiple follicular cyst, giant cell tumor (local and general in origin), fibroma, fibrosarcoma, osteogenic sarcoma, and metastatic carcinoma (breast and thyroid).

The diagnosis of an ameloblastoma or of any other tumor of the mandible should not be made by means of the roentgenogram alone. There can be a wide variation in the roentgenographic findings of different ameloblastomas and they may simulate other tumors. And conversely other tumors of the mandible may simulate the ameloblastoma on the roentgenogram.

The primary value of the roentgenogram is to demonstrate the site and extent of the multilocular lesions of the mandible.

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THE CHERNEY INCISION AS APPLIED TO THE SURGERY OF THE LOWER URETER AND BLADDER

DONALD R. SMITH, M.D., San Francisco, California

WHILE the suprapubic midline or low rectus incisions afford good exposure for most procedures directed toward the bladder and lower ureter, instances occasionally arise in which these approaches seem inadequate, particularly for surgery of the deep extraperitoneal pelvic zone, the extensive dissection necessary for total cystectomy, or for surgery of the vesical neck or subsymphyseal urethra. A transverse low abdominal incision has been recently described by Cherney which allows of extensive exposure of the lower portion of the peritoneal cavity for surgery of the lower bowel and female reproductive organs. This incision, which is readily applicable to urologic procedures, is described in the following paragraphs.

From the Division of Surgery, Subdivision of Urology, University of California Medical School, San Francisco

Read at the annual meeting of the California Medical Association in Los Angeles on May 7, 1945.

The transverse skin incision is curved slightly, with its convexity directed downward, and extends from just medial and inferior to either anterior superior spine of the ilium (Fig. 1). The wound thereby passes through the upper pubic hair line, often following a normal skin fold, and is carried down to the aponeurosis of the external oblique muscles and the sheaths of the rectus. At either extremity of the incision the superficial epigastric vessels are encountered and one or both may be sacrificed for added exposure.

The sheaths of the rectus are then opened transversely in line with the skin incision and the internal and external oblique aponeuroses are next incised to the angles of the wound. In this portion of the incision, the internal oblique muscle becomes fleshy but, since its fibers run in line with the wound, the muscle may be split further by blunt dissection. Occasionally the transversus muscle is present

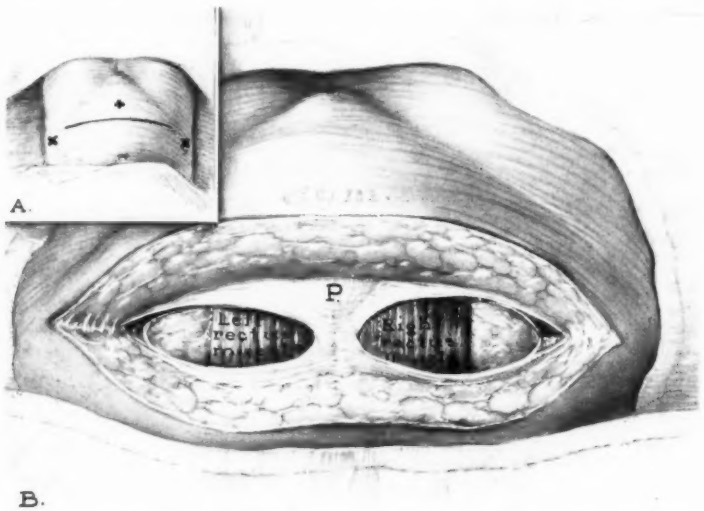


Fig. 1. The incision through the skin, sheaths of the recti, and lateral abdominal muscles. *P*, designates pyramidalis muscles under linea alba.

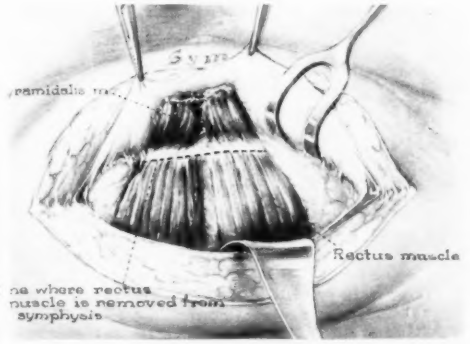


Fig. 2. The completed transverse incision. The pyramidalis muscles are separated from the underlying recti. The rectus muscles are transected through their points of origin on the pubis.

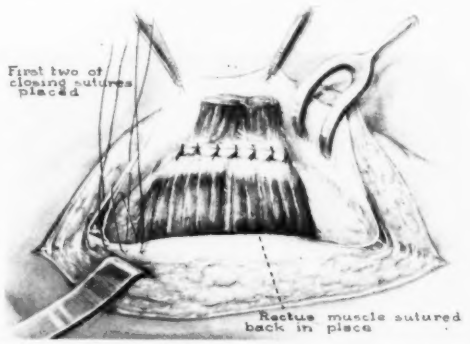
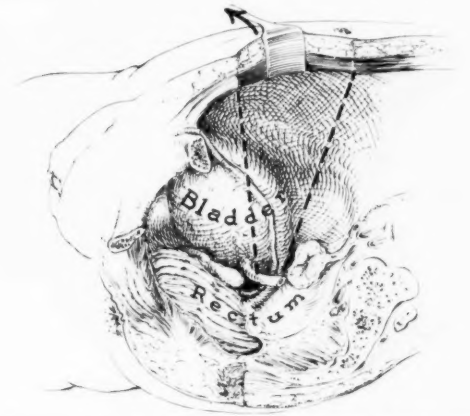


Fig. 3. Closure. The tendinous edges of the rectus muscles are resutured to the symphysis or under surface of the rectus sheath. The lateral abdominal muscles and the sheath are closed in one layer with interrupted sutures.

in the lower abdominal wall and then it also must be opened. This exposes the rectus muscles in the midline and the transversalis fascia and underlying peritoneum laterally.

Traction is next applied to the inferior flap of the sheath of the rectus and by gauze dissection it is freed from the underlying rectus muscles down to the symphysis pubis. A central fibrous septum extending from the under surface of the rectus sheaths to the recti must be cut and the pyramidalis muscles freed from the anterior surface of the rectus muscles (Fig. 2). The inferior ends of the recti then are separated from the underlying transversalis fascia and it will be noticed that they become largely fibrous or even completely tendinous at their points of origin. The rectus muscles are cut off flush with the pubic bone, their tendinous ends being preserved for later resuture. The recti then retract well up to the upper border of the sheath of the rectus, exposing an elliptical space averaging 7 inches by 5 inches in its transverse and vertical axis respectively, an area twice that afforded by the midline incision and with its transverse axis much closer to the symphysis pubis than that of the latter. The transversalis fascia is then opened and the surgeon is prepared for wide exposure of the bladder or lower ureter.

Fig. 4. a, left. Exposure gained with Cherney incision allowing excellent access to the deep extravesical space.



Compare with the limited exposure afforded by the vertical midline incision, b.

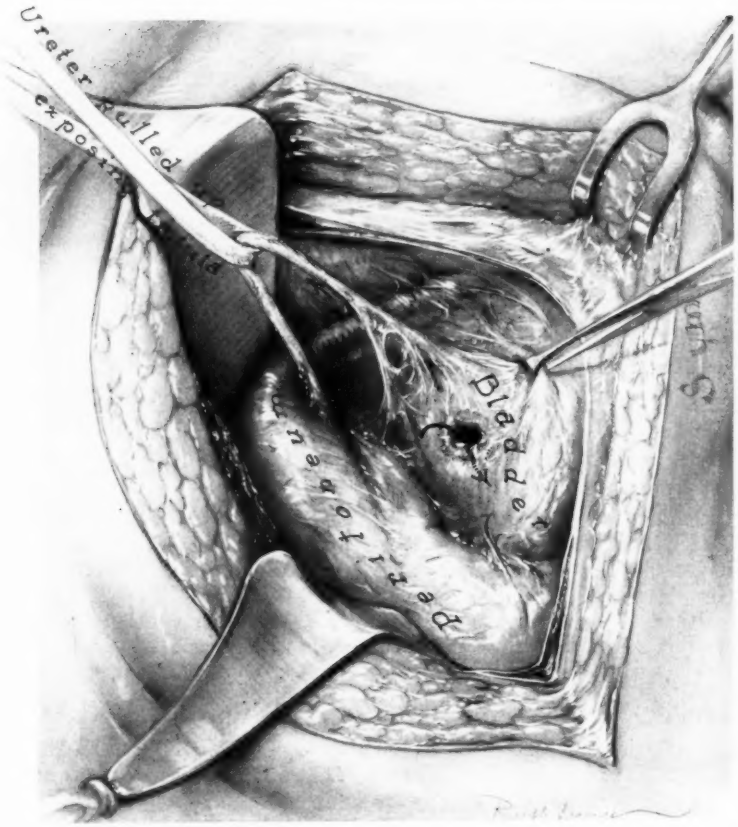


Fig. 5. Repair of vesicovaginal fistula adjacent to left ureter. Fistula excised and both vaginal and vesical openings easily inverted.

In the closing of the wound, the tendinous ends of the rectus muscles are first resutured to the under surface of the lower flap of the sheath of the rectus at or near the symphysis (Fig. 3). While considerable tension upon this suture line might be expected, it must be remembered that the rectus muscle is strongly attached on its anterior surface to the anterior sheath of the rectus by three or more transverse tendinous intersections so that when the transverse incision through the aponeuroses of the lateral abdominal muscles and rectus sheaths is sutured, the sheath itself takes the tension of the upper two-thirds of the muscle. Drains may be brought out through the incision or through a stab wound.

Certain advantages which this incision offers suggest its employment for selected surgical procedures: the transverse wound is longer than the vertical incisions so that exposure is increased. Vertical wounds give limited exposure because of the convergence of the sheaths of the rectus muscles at either angle of the wound even with strong lateral retraction. The Cherney incision gives excellent exposure at the plane of the symphysis overlying the deep pelvic zone (Fig. 4). The transverse wound is a strong wound. No muscle is denervated, the lateral abdominal muscles and the recti are divided at different levels, less retraction is needed, and lighter anesthesia therefore can be used. The direc-

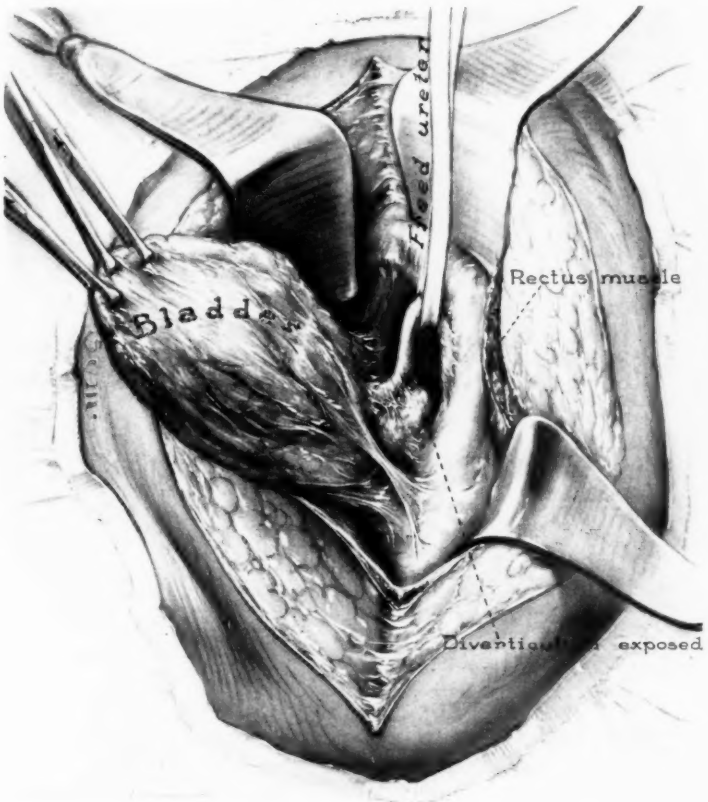


Fig. 6. Excision of vesical diverticulum posterior to right ureter. The use of the Cherney incision greatly facilitated its removal.

tion of pull of the oblique muscles with strain is parallel to the direction of the incision in their aponeuroses and all sutures are taken through fascia which makes for good healing, thereby decreasing the incidence of hernia.

CASE REPORTS

The following cases are presented to demonstrate the exposure obtained through this approach:

A woman, aged 20 years, developed a vesicovaginal fistula following instrumental delivery of a stillborn hydrocephalic baby. Examination 8 months later showed the fistulous opening to be just lateral to the badly lacerated cervix and cystoscopy demonstrated the opening in the bladder to be 1 centimeter medial to the left ureteral orifice. Because of the proximity of the fistula to the left ureter, an approach affording good visualization of the area was deemed advisable, so a Cherney incision was used. After its identification in the region of the pelvic brim, the ureter was followed down to the bladder (Fig. 5), the bladder was opened, the fistulous tract excised, and the openings in both the vagina and bladder were closed by interrupted inverting sutures. A cystostomy tube was left in place for 10 days, and 2 weeks after surgery was performed the patient was voiding without vaginal urinary leakage.

A man, aged 60 years, had previously undergone transurethral prostatic resection but troublesome symptoms from persistent pyuria continued because of vesical diverticula in the region of the right ureteral orifice. Diverticulectomy was decided upon and the transverse incision was used because of the excellent exposure of the trigonal area which it affords (Fig. 6).

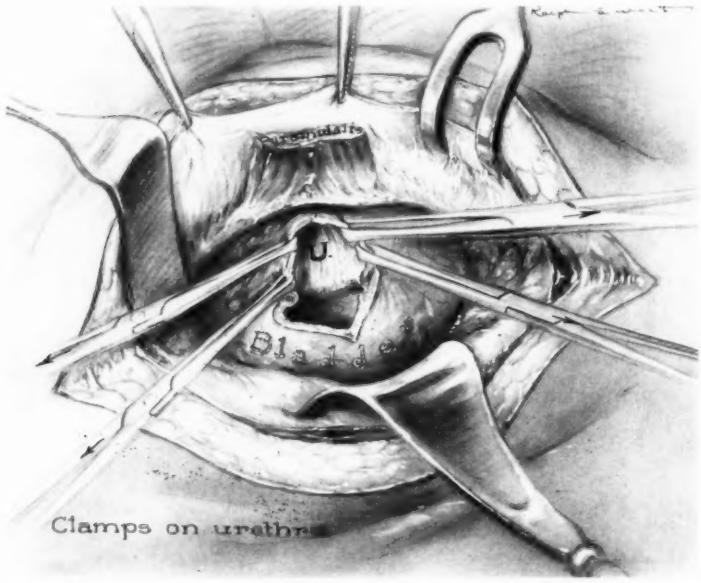


Fig. 7. Resection of anterior half of urethra, *U*, bladder neck, and adjacent bladder wall for congenital defect of sphincter. In the closing of this defect, the distal suture in the urethra was easily placed even though it was situated below the inferior border of the symphysis pubis.

A girl, aged 6 years, complained of enuresis since birth as well as incontinence during the day. Renal function and urinalysis were normal. Cystoscopy demonstrated a markedly relaxed urethrovesical sphincter and a patulous urethra. The anal tone was intact. Neurological examination revealed no sensory or motor changes and intravenous urograms were normal. Roentgenograms of the bones of the lower spine and pelvis showed them to be normal except for separation of the symphyseal rami by a distance of 1 inch. This suggested the probability of an anterior defect of the vesical sphincter such as one might observe in a minor degree of exstrophy, so it was thought advisable to explore the neck of the bladder and the urethra. Exploration was done through a Cherney incision with admirable exposure resulting (Fig. 7). The anterior half of the urethra and vesical neck were resected and the remainder closed, the deepest suture being placed inferior to the lower border of the symphysis pubis under direct vision.

The results obtained for these patients might not have been as satisfactory if an approach offering less exposure had been chosen. One of the fundamental rules of good surgical technique is to gain adequate exposure. The Cherney incision fills this requirement in a superior manner.

SUMMARY

1. The Cherney incision offers excellent exposure of the extravesical trigonal area (juxtavesical stone, diverticulum of the bladder, vesicovaginal fistula, etc.), vesical neck and subsymphyseal urethra. It is peculiarly suited for total cystectomy.

2. The technique of the approach is described.

3. Cases are presented which illustrate its advantages.

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THE EXPOSURE OF HIGH LESIONS OF THE SCIATIC NERVE

IAN AIRD, Ch.M., F.R.C.S. (Ed.), Edinburgh, Scotland

THE inadequacy, difficulty, and danger of the classical nineteenth century approach to the structures under cover of the gluteus maximus through an incision in the line of its fibers were exposed by Tiolle and Delmas, whose trapdoor elevation of the gluteus maximus can now be regarded as the standard procedure. A similar technique was described by Stookey, whose question-mark incision later authors have adopted. Henry has recently elaborated the operation, and has described its steps with a wealth of anatomical detail and argument which could hardly be more complete. In this paper a full description of the operation will not be attempted, but during the recent war certain problems in the management of high lesions of the sciatic nerve have emerged, and the measures devised to solve these may be added to the operative procedure.

The main difficulties encountered in the repair of a lesion of the sciatic nerve at its emergence from the pelvis are four in number: (1) hemorrhage from the branches or the main trunk of the inferior gluteal vein; (2) retraction of the neuroma into the pelvis; (3) inability of the nerve to rotate for the insertion of the anterior layer of sutures; and (4) liability of the posterior cutaneous nerve of the thigh to injury, not when the fascia of the thigh is incised initially, but when it is closed at the end of the operation. How these difficulties occur and how they can be overcome, are best illustrated by a brief description of the operation.

The incision (Fig. 1). With the patient prone and the knee pillowed to hyperextend the hip, the incision is begun at a point on the crest of the ilium a handsbreadth in front of its posterior superior spine, and the knife is drawn down to the tip of the greater trochanter, over the lateral aspect (not the posterior edge) of the trochanter, and then in a curve inward to the junction of the gluteal fold with the posterior axial line of the thigh. From this point the incision passes vertically downward toward or into the popliteal fossa as far as may be required for the adequate mobilization of the distal segment of the sciatic nerve.

From the Department of Surgery, University of Edinburgh; and the Peripheral Nerve Unit, Gogarburn E. M. S. Hospital, Edinburgh.

Division of fascia. In the lower (vertical) part of the wound the fascia of the thigh is incised parallel to and just lateral to the posterior cutaneous nerve of the thigh, whose white outline is clearly visible through the fascial sheet. The lower edge of the gluteus maximus is defined between the point of emergence of the posterior cutaneous nerve of the thigh and the femoral insertion of the muscle.

Mobilization of the gluteus maximus. In the outer part of the wound, a vertical incision is made down to the lateral surface of the greater trochanter through the iliotibial tract. This provides the most convenient access to the space deep to the gluteus maximus; elsewhere a subgluteal plane of cleavage is difficult to identify. A finger in-

Fig. 1. Incision.

Fig. 2. Division of insertion of the gluteus maximus.

Fig. 3. Elevation of the gluteus maximus: division of tendon of piriformis. Note the spread eagle stretching of the branches of the inferior gluteal vessels, and the risk of tearing at the multiple bifurcations between them.

serted through the fascial incision can be readily passed upward under the junction of the upper fibers of the gluteus maximus with the iliotibial tract, to serve as a director for the knife (Fig. 2). This incision continues upward to the superolateral border of the gluteus maximus, and then along that border, dividing the iliotibial tract and freeing the superolateral border of the muscle completely. Now that the superficial portion of the gluteus maximus is mobilized, all that remains is to pass a finger upwards from the outer end of the lower border of the muscle, close to the femur, and to divide the muscle fibers of the deeper part close to their insertion into the femur.

Retraction of the gluteus maximus: division of the piriformis (Fig. 3). A broad-bladed retractor elevates the gluteus maximus upward and medially to expose the piriformis and the structures emerging from the cover of its lower border, but the initial elevation of the muscular trapdoor must be gentle, for as it is retracted, the branches of the inferior gluteal vessels passing to its deep surface are pulled dangerously taut. This danger is implicit in the observation of Fiolle and Delmas (p. 45 of the English translation) that "the superficial branches of the gluteal vessels which supply the muscular mass become tense, like cords, between the sciatic notch and the under surface of the upraised muscle." The main trunks of the inferior gluteal vessels are relatively fixed by the lower border of the piriformis, and sometimes absolutely fixed by scar tissue at their emergence from the pelvis, and tributaries of the gluteal vein may be torn. Bleeding is particularly obstinate if one of the muscular tributaries is torn from the parent trunk, or if two converging tributaries are pulled apart to provide a longitudinal rent splitting the parent trunk; such bleeding may be almost uncontrollable if the torn proximal end of the vein is fixed in the sciatic notch by dense scar tissue. However, if the tendon of the piriformis is now cut across close to its insertion (Fig. 3)

Fig. 4. Piriformis retracted with the gluteus maximus. Tension on the inferior gluteal trunks is lessened, a greater length of these trunks is exposed. The companion vessels of the sciatic nerve, and a laterally passing branch of the inferior gluteal trunk, have not yet been divided; their division will still further lessen the tension on the muscular branches. Note the additional length of the proximal cut end of sciatic nerve exposed by division of the piriformis.

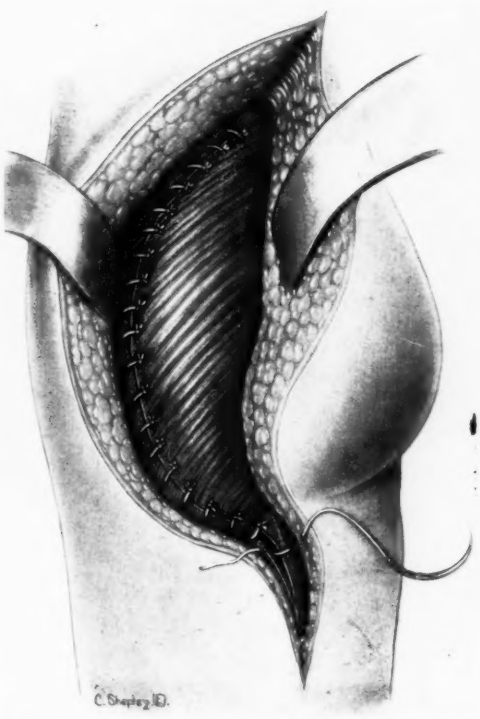

Fig. 5. Suture of the gluteus maximus. Note the needle picking up the fascia of thigh clear of and well medial to the line of the posterior cutaneous nerve.

cleared at its margins by blunt dissection, and elevated by a rake retractor in the same direction as the gluteus maximus, some additional mobility is afforded to the main trunks of the inferior gluteal vessels (Fig. 4), and the anastomosing branches which course upward over the surface of the piriformis to meet the descending branches of the superior gluteal vessels are retracted in the same direction as the superior muscular branches. Even if bleeding occurs now, a substantially greater length of the main gluteal vessels is available for ligature. An additional safeguard against hemorrhage is the formal ligation and division of the companion vessels of the sciatic nerve, and any laterally directed branches of the inferior gluteal vessels. The former and one of the latter are shown undivided in Figure 4; if they are divided before the trapdoor is fully raised, there is less risk of tearing at their V-junctions with the branches to the gluteus maximus.

Figure 4 shows a further advantage of the division and elevation of the piriformis—wider access to the proximal cut end of the divided sciatic nerve. In 3 patients with sciatic nerve lesions treated in 1945, the nerve had been wounded at such a high level, and its proximal end had retracted so far into the sciatic notch, that only the distal extremity of the neuroma could be drawn from below the piriformis. Division and elevation of the piriformis in each of these cases afforded access to just these few extra millimeters of the sciatic trunk which were necessary for trimming and suture. In 1 case suture was performed at the level where the nerve was beginning to broaden in its parent plexus.

Technique of anastomosis. If the normal technique of nerve suture is followed at this level, and the superficial row of sutures is inserted first, it

will be found impossible to rotate the nerve sufficiently for insertion of the second (anterior) row. The anterior row, on the far side of the nerve from the operator, must be completed before the posterior (superficial) row is begun.

Closure of the wound. After suture of the piriformis, and of the gluteus maximus muscle by interrupted stitches, the fascial wound in the back of the thigh is closed. The posterior cutaneous nerve of the thigh is liable to be included in this fascial suture; easily visible through the unopened fascia at the beginning of the operation, it is much less distinct as it lies under the cut fascial edge at this late stage. Inclusion of the nerve in the suture can be avoided by picking up the medial sheet of fascia well away from its edge (Fig. 5) so that when drawn taut the stitch or stitches lie superficial and medial to the line of the nerve.

SUMMARY

The advantages of dividing the piriformis muscle in the exposure of high lesions of the sciatic nerve are discussed, and other and minor modifications of the operative exposure of the deeper structures of the buttock, as it has been developed by Fiolle and Delmas, Stookey, and Henry, are suggested.

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CINEPLASTIC FOREARM AMPUTATIONS AND PROSTHESES

B. K. RANK, Lieutenant Colonel, A.A.M.C., and G. D. HENDERSON, Major, A.A.D.C.

THE problem of substitution for a lost part is paramount in the case of the upper limb amputee. Any artificial arm compares badly with its counterpart for the lower limb in both purposes of a limb prosthesis—to hide the defect and to provide a maximum restoration of function. The absence of an arm is obvious to the casual observer in the street. Whereas few lower limb amputees are grossly manifest as such, in the case of those who have lost an arm it is a different and sad story; we see more with their coat sleeves tucked into their pockets than we see wearing an arm prosthesis of any sort.

No man-made mechanism can or ever will reduplicate the innumerable intricacies which subserve the prehensile function of the human hand. We must accept this or else we become fatalistic when assessing the value of any hand prosthesis. It must never be compared with the normal. It can be fairly judged only in comparison with other types of prostheses, or with the limb stump devoid of any prosthesis at all.

We can examine the reason for the widespread disregard for upper limb prostheses in relation to their two functions:

1. As esthetic substitutes. It is easy to understand why an arm amputee bothers little about a prosthesis for its esthetic value. Most such prostheses are of wood, or of metal, and they look wooden or metallic. They are, indeed, well covered by a glove, as in the standard dress arm. In certain phases of daily life, this may be adequate, but for just as many—indoors, for example—it is not. A poor camouflage value does not compensate for their nuisance value. It helps little in deciding the moral conflict of the amputee as to whether he should display or hide his disability.

If the external appearance could be more adequately presented, it would be a different story. Much of the true handicap of the amputee arises from the way he is noticed and regarded by society in association with some general idea of unproductiveness or dead-endedness. Unfortunately, it is this attitude which is easily reflected and inculcated in the man himself as an amputee personality. Were it not for this, the physical, moral, and vocational disability of a man who has lost a limb might not be as gross as popular idea would have us believe.

2. As functional substitutes. In this, the main regard, prostheses vary widely, not only in the different types available, but particularly in their application to an individual. It is this individual factor which makes the evaluation of any particular type of prosthesis so difficult. It also necessitates personal contact and understanding of each patient if management is to provide him, as an individual, with the best type available. There are, of course, limits of practical uniformity and financial consideration.

It is not the purpose of this communication to detail the various types of prostheses which are available—they have a long history. They range in mechanical complexity through the ages of their development from simple useful iron hooks as made by an amputee himself or his artisan friend, to some of the most elaborate unwieldy mechanical contraptions which have ever been made experimentally or hopefully by limb makers.

The more simple arm prostheses may be described as of "passive type," i.e. nonmobile attachments to ordinary limb or bucket fixtures. The ordinary hook as widely used is one of these; but there are many and more complicated attachments, some of which—although grotesque in appearance—have enormous application in particular cases. We must not let the more ugly of these museum pieces distort our sense of proportion, for with simple attachments to forearm buckets, an amazing degree of self-help and activity can be effected by some.

From the No. 2 Facio-Maxillary and Plastic Surgery Unit, Attached 115 (Heidelberg) Military Hospital, Melbourne, Australia.

In contrast to the "passive types" are the "active types" of prostheses, the parts of which are activated in varying degree by muscle movement. Their many types conform to two main groups:

a. Some utilize the extraneous muscle movement in relation to remaining joints to effect movement in the prosthesis. Most of these rely on a development and practice with the same or opposite shoulder movement. The standard cleft hook is well known of this type, and Carnes' arm is probably the best of the many designs on this principle. Many others have become scrap metal. All employ strings, pulleys, cords, or wires which require unnatural action or motion for a function which does not fully duplicate hand movement. In general, their cumbersome action tallies badly with their nuisance value to all and what to most implies a hopeless range of personal endeavor, training, and concentration to make them effective.

b. The other main group of active prostheses involves the principle and subject of cineplasty.

Cineplasty. Cineplasty implies utilization of the muscles actually within an amputation stump to impart some of their normal function to an appropriate prosthesis. It requires some type of surgical operation on the stump by which the unused and wasting source of muscle potential is utilized. Function is produced in a way which cannot be achieved by other methods, for direct control of the mechanism can be effected by the same muscle groups which would normally be producing that same action in a hand. Normal psychomotor patterns are involved. There is no latent period of inertia in activating or training extraneous muscle groups, and the patient has encouragement in the first use of a cineplastic prosthesis. We must remember, however, that cineplasty implies a mechanical prosthesis, still with a nuisance value, a necessity for maintenance, and an absence of tactile facility.

The principle of cineplasty was elaborated about 1896 as a theory, by the Italian physician, Vanghetti. He was thinking for the mutilees among Italians fighting in Abyssinia at that time. Vanghetti himself did only experimental work, mainly on birds. It was long before he could convince one of his compatriots—one Ceci of Pisa—to do the first human cineplastic operation. Such procedures, however, had no effective trial until the mutilees of the 1914-1918 war had accumulated. Then Sauerbruch in Germany and the Italian school at Bologna (Ceci, Putti, Galliazzi) did large numbers of these operations in special clinics where there was apparently a very close liaison between surgeon and prosthetist. The few references in British literature are either by extraneous observers at these clinics or by the Continental men themselves. There were sporadic and isolated trials by individual surgeons, but the method received no general acceptance or favor. American writers have been more enthusiastic—Kessler, who studied in the Sauerbruch clinic, is apparently a practiced exponent and advocate of this principle.

A necessity for the highest order of teamwork explains the apparent discrepancy; why cineplasty has achieved a success and favor only in special clinics where large numbers are done, and not in sporadic trials among isolated cases. The basic organization in the special plastic surgery clinics throughout British and Imperial countries, thanks to the teaching and inspiration of Sir Harold Gillies, has offered unusual scope for such teamwork. In this Unit, attached to a large city base hospital, and where we have extended our prosthetic facilities beyond the usual, we have thought fit to evaluate for ourselves—by a limited first hand trial—something of the place of cineplasty for the upper limb amputee. In so doing, both concerning the plastic operation involved and the prosthesis used, we have endeavored to make improvements in what we could discern of their more obvious shortcomings. This work has so far been confined to forearm cineplasty and our present conclusions are epitomized in two chapters: (1) The plastic operation involved, (2) The prosthesis used.

THE PLASTIC OPERATION

There are many ways in which the muscle function of an amputation stump can and has been tapped. Sauerbruch's method has apparently best survived the sieve of time and trial. By it, a skin lined canal is made through

individual muscles or groups of muscles in a stump. Through these canals are inserted pegs, the movements of which are transmitted by appropriate mechanism of a prosthesis to produce movement of an artificial hand.

The permutations of procedure which could be applied to the making of a skin lined tube through muscle are many, but in view of the work of such a skin tube, we consider the following general principles should be satisfied in its making:

a. The tube must be a soundly healed and stable structure.

b. Any local operative procedures involved should create a minimum of scar formation which is likely to embarrass mobility of the tube.

c. The stump to which the prosthesis has to be fitted should be left devoid of anesthetic areas, areas of vulnerable scar, and wherever possible devoid of free skin grafts. Free skin grafts on an amputation stump are not always a satisfactory proposition. They are potentially unstable with petty trauma and they become adherent to deep structures in some degree. If a free graft has to be used, it should not overlie the area of muscle transfixion or the end of the stump.

With these factors in view, one of us (B.K.R.) has evolved an effective cineplastic operation which can be done simultaneously with an amputation or reamputation. The muscle tube is made of a skin and fat flap, its line of suture is off the line of pressure of the transfixion rod. It is a one stage operation in which free skin grafts are not used, and which is devoid of undue risks with flap vitality.

This operation can be done without modification only where there is sufficient length of limb for the use of the skin flaps from the region to be amputated. We would emphasize on this basis alone, the value always of the most conservative primary upper limb amputations which would render such a subsequent procedure possible and satisfactory. If remaining length of limb does not permit of the operation, a compromise in the method is required, and use of a supplementary free skin graft may be necessary. Chief of the modifications we have used will be indicated after the one stage operation is described.

Cineplastic reamputation. The stages of cineplastic reamputation are best followed in reference to Figure 1.

1. Surface markings (Fig. 1, a) XX' is the line of election for constructing a skin canal through the superficial plane of forearm muscles. It represents the junction of the middle and distal thirds of the middle third of the full length of forearm. It is drawn at right angles to a line from the medial epicondyle to the midvolar wrist in the case of the flexor group, or a line from the lateral epicondyle to middorsal wrist in the case of the extensor group of muscles.

This line XX' respects two primary anatomical considerations as pointed out by all exponents of Sauerbruch's principle: (a) The strongest available potential of muscle power and excursion is at the region where contracting muscle belly gives place to passive tendon. In the forearm, this potential is approximately in the distal third of its middle third. (b) The superficial forearm muscle groups have a slightly oblique set on account of their essential origins from the humeral epicondyle regions. This fact must be remembered so that the tubes are made through the muscles, exactly at right angles to their direction of pull.

These facts are best verified and marked before operation with a co-operative patient.

The line XX' is only an approximate estimate and because of unpredictable variations in individual amputation stumps with varying degrees of muscle retraction, we consider it best to approach this line with a demilunar skin incision YY' which will allow some variation of XX' according to exact findings. It will also ensure that there is no potential scar to become adherent to the muscle over its line of canalization.

Identifying and canalizing the muscles (Fig. 1, b, c, d). After the skin flap YY' is raised the deep fascia is incised and the superficial plane of muscles is identified. The flexor muscles selected for canalization are the flexor digitorum sublimis (superficial portion) and the flexor carpi radialis, both of which can be transfixed in the same plane. The main mass of the flexor carpi ulnaris is usually too far posteriorly to be included.

It is important to ensure that the tube actually passes through muscle substance—it is easy to slip in between muscle planes. In the first instance, transfixion is conveniently effected under careful vision, a pair of eye scissors being used (Fig. 1, c). This line of muscle transfixion is then dilated by successive passage of a special set of graded and interlocking solid metal dilators (Fig. 1, d). On the two larger of these can be fitted and passed through the muscles bored hollow metal tubes which measure ½ inch by ⅝ inch. The smaller tube is used for small limbs or if further dilation proves difficult. The appropriate hollow tube is left *in situ* as a dilator while the skin tube is being made.

3. Designing and making the skin tubes. On the ulnar side of the forearm, a rectangular skin flap *ABCD* is designed (Fig. 1, e) with its base *AB* obliquely across the transfixion line *XX'*, its sides parallel, and its dimensions depending on the length and bore of the muscle canal. In an average case, this requires a flap approximately 2¾ inch by 1½ inch.

After the flap is carefully raised on the base *AB* (Fig. 1, f), it is turned in to make a skin lined tube. This step is facilitated by first inserting at each end an inverted end on mattress stitch, tied with knots on the skin surface. These are used as stay stitches. One stitch coapts *C* and *D*, but the other must be sufficiently distant from *A* and *B* to allow the skin edges to come together without undue tension (Fig. 1, g). After an appropriate size rubber tube is inserted, the skin lined tube is completed by a continuous subcutaneous running stitch which is first tied to the near stay stitch and finally to the far stay stitch (Fig. 1, h). An assistant holds appropriate tension in the continuous stitch during its insertion. Fine silk on an atraumatic needle is used.

4. Passing the skin tube through the muscle canal. With the aid of a pair of sinus forceps passed down the metal tube from the end opposite the base of the skin tube, the stay stitch and rubber tube at its free end are guided into the near end of the metal tube which should not be projecting far beyond the muscle opening on that side (Fig. 1, j, h). The skin tube is then drawn carefully into the metal tube. On removal of the metal tube from the far side, the skin tube is left *in situ* through the muscles (Fig. 1, i). This method radically simplifies what is otherwise a very tedious procedure.

5. Completing the skin tube. The initial exploratory flap is then resutured in place and the open ends of the skin tube are carefully sutured all around their margins to outside skin.

On the dorsum of the forearm, the same procedure is repeated in complementary design. The extensor digitorum communis and extensor carpi ulnaris muscles are used, but the canal is usually slightly shorter than that through the flexor muscles. In this case, the flap used for making the skin tube is designed on the radial side of the forearm.

When both tubes are completed, there remain two secondary defects which are the donor sites of the skin tubes—one on the ulnar side of the volar aspect, the other on the radial side of the dorsal aspect of the forearm.

The Reamputation

Two amputation flaps are raised on lateral bases, but contain skin from the volar and dorsal surfaces of the forearm respectively (Fig. 1, j, k, l).

The anterior flap *EFGH* is raised on an oblique base *EF* on the radial side of the limb. It consists essentially of volar skin. The posterior flap *JKLM* is conversely raised on an oblique base *JK* on the ulnar side of the limb and it consists essentially of dorsal skin.

It will be noted that each of these flaps consists mainly of the skin distal to the raw areas. When rotated in opposite directions they close these areas as well as the site of reamputation.

These flaps must be designed very accurately and carefully. The skin areas proximal to their base lines *EF* on the radial side and *JK* on the ulnar side as represented by the shaded areas on Figure 1, j, k, l, might well be described as "the critical areas." There must be no undermining of skin edges in this region, on which depends the existence of the flaps. This step constitutes one of the main points of the operation. The free distal end of the one flap is on the margin of the critical area of the other flap.

After the flaps are raised, the muscles are divided at a level as far proximal as the bases of the flaps will allow, care being used not to jeopardize their blood supply further (Fig. 1, l). After proximal traction on the severed muscles, the bones are divided at a level slightly proximal again to the severed muscles.

After routine hemostasis is effected, the deep muscles are sutured over the dorsal ends, but the superficial groups which have been canalized are left free to retract.

Final Suturing

Rotation of the volar and dorsal flaps in opposite directions (Fig. 1, m) allows each to close the donor site of the skin tube on its respective aspect without undue tension, and the distal curved margins of each flap are sutured one to the other over the amputation site. This method makes a curved suture line in a coronal plane around the end of the stump.

Silk sutures are used throughout with every precaution and finesse for accurate edge-to-edge apposition.

The final arrangement and suturing is shown in Figure 1, n, o, p.

Rubber tubes are left through the skin tubes, but they must not be too large and tight.

A routine dressing and light crepe bandage pressure is arranged over the whole stump. This is left undisturbed for a week.

Postoperative Management

At the first dressing, 1 week after operation, half the superficial stitches are removed. The rubber tubes are removed from the skin tubes. The continuous stitch through the length of the skin tube is carefully identified from its fixation to the two separate end stitches, and all are carefully removed. If the running stitch feels tight, it is left a few days longer.

Through the skin tubes are then passed acrylic rods made to appropriate diameter. It is important to see that for a time these are always passed from the base side of the skin tube flaps and removed from the opposite side.

Remaining sutures are removed a few days later, after which the rods are removed daily for routine toilet of the skin tubes.

Healing should be complete in from 2 to 3 weeks, when voluntary active contractions of the appropriate muscles are commenced. Function is slowly increased, and after another 2 weeks, exercising against increasing resistance is arranged as in Figure 2. Exercise is continued until adequate force and excursion are developed when the appropriate prosthesis is fitted. Average excursion is ½ inch to ¾ inch for the flexor rod and ⅜ inch to ½ inch for the extensor rod. The final result and appearance is shown in Figure 3.

Variations from the Described Operation

It is obvious that the one stage cineplastic reamputation implies an adequate length of amputation stump, i.e. more than ⅔ of the forearm must be present, otherwise there is insufficient local skin flap available for the operation described without undue tension.

For stumps already too short for the cineplastic reamputation as described the following may be necessary:

1. In most of these cases it is usually necessary to use a free skin graft on the donor site of the skin tubes. As a free graft on an amputation stump is always a vulnerable area, if one has to be used it should not be placed over the end of the stump, nor do we consider it should be over the muscle tubes where its contraction and associated scar would embarrass the desired function of the tube. This point we consider the main disadvantage of the simple and commonly used method of making a skin tube through muscle as practiced by Sauerbruch and advocated by Nissen and Bergmann in their excellent monograph on this subject. If a free graft is required, the skin tube can be made exactly as described in the elective operation, and the secondary defects grafted as they stand with thick split skin (Fig. 4). In one case, contraction of the graft did produce a bad distortion of an extensor tube which had to be abandoned.

2. *The single tube operation.* In some cases, rearrangements of the amputation flaps will permit of making one skin tube without resort to free grafts. In 2 cases, a well functioning flexor tube has been made and the prosthesis modified accordingly so that a light spring takes over the function of the extensor mus-

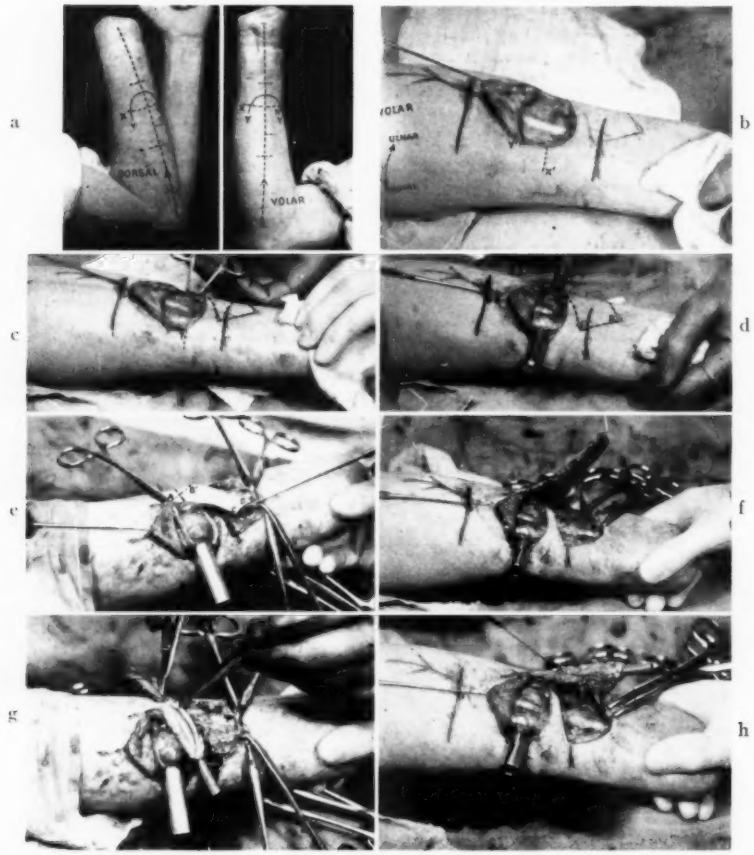

Fig. 1. a to h, Stages and technique of cineplastic reamputation of forearm.

cles. The possible advantages of this more simple procedure are still open to consideration and will be considered later.

3. Use of abdominal flaps. Some stumps still shorter, though still adequate for cineplasty, may not permit of free local use of skin for making skin tubes. Local scarring might also produce this same consideration. It may then be necessary to design and evolve skin tubes from other body regions in a staged operation (Fig. 5).

Disadvantages associated with any of these variations reiterate the advantages of the one stage cineplastic reamputation as described and again call for every effort to conserve always the maximum length of upper limb in primary surgery of injury.

THE PROSTHESIS

In an endeavor to reduce some of the usual deficiencies pertinent to normal upper limb prostheses and other cineplastic mechanisms we have concentrated in three main directions.

a. The outward esthetic appearance. It is considered that with the modern materials available, some better replica of the normal hand should be possible which would ensure its continued use on this score alone.

b. An efficient, intrinsic mechanical leverage system—to transmit the muscle power to move

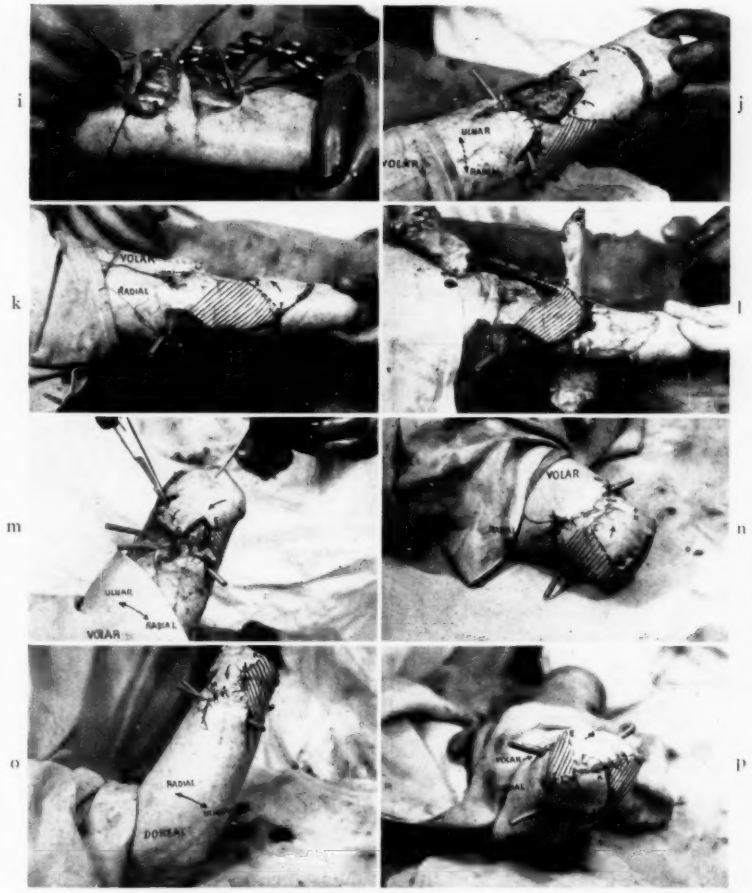

Fig. 1, i to p.

ment of artificial fingers in the most effective way.

c. Reduction of the total weight of the prosthesis—to well below ordinary standards.

To such ends, in 2 years of experimental construction and trial, in relation to a small series of selected cases, taking advantage of modern materials available and with many variations in their use and construction, we have elaborated a satisfactory working principle and prototype.

This forearm cineplastic prosthesis, which we call the Heidelberg pattern, is depicted in Figure 6. Its general mechanical arrangement and assembly is shown in Figure 7. Full details of all its essential parts are beyond the scope of this report, but its essential features will be expanded "seriatim" relative to (a) the hand superstructure; (b) the intrinsic mechanism; (c) the accessory fittings.

The Hand Superstructure

The hand superstructure is made in acrylic (methyl methacrylate) resin, as a hollow casing which minimizes weight and provides space for the mechanism. Acrylic was selected for its lightness and a transparency which renders it suitable for realistic color effects beyond that of ordinary materials previously used. In order to produce the exact replica of

Fig. 2. Mechanism used for exercising muscles following cineplastic amputation. Note arrangement of transfixion rods, stirrups, and tension spring.

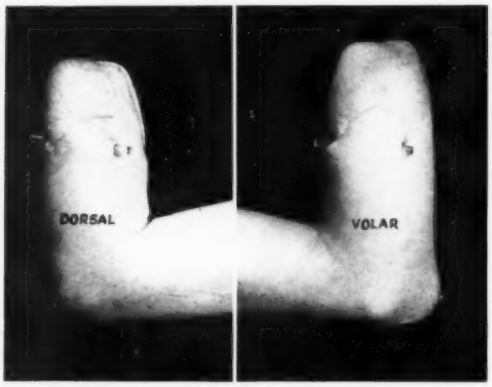

Fig. 3. Final appearance of stump, 3 months after a one stage cineplastic operation.

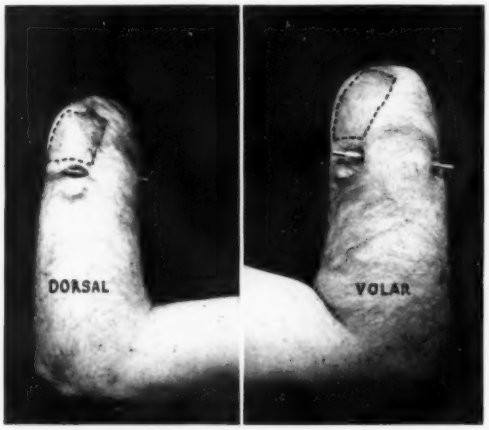

Fig. 4. The dotted outline indicates placing of free skin grafts on secondary defects of skin tube flaps. A method used when length of stump does not permit of the described operation.

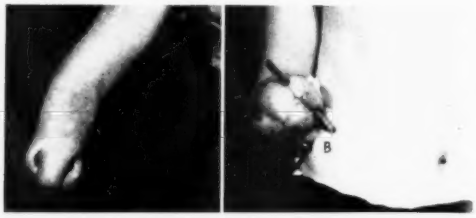

Fig. 5. Skin tubes made from direct abdominal flaps i a two stage operation. This method may be necessary wit very short or scarred stumps. b, Tube flaps are still at tached to abdomen.

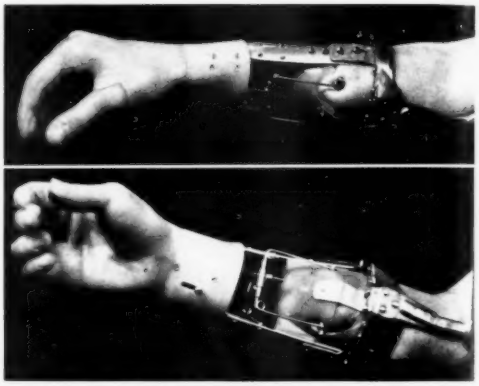

Fig. 6. The "Heidelberg" prosthesis as it appears fitted to an amputation stump.

a normal hand, full impressions were first made from selected normal hands with a hydrocolloid impression material.[1] From these impressions, models of the hand were made in artificial stone.

The acrylic hand casing is made in 10 separate segments. Each of these segments is made in a die of plaster prepared from appropriate pieces of the stone model which is fragmented as shown in Figure 8. Use of a special tubular saw, illustrated in the same figure, permits of cylinders being taken out of the bases of both the thumb piece and the two adjoined opposing fingers. These regions constitute the only two ultimate moving joints of the prosthesis. The ring and little fingers are dummy.

[1] *Impression technique.* Two ounces agar agar, 3 pints of water, small piec of soap (the size of a marble), a handful of cellulose wool. Boil the wat and pour over the Agar (cut agar into small pieces). Boil mixture i double saucepan until dissolved. Add soap and cellulose wool, stirri well. Remove mixture from flame, allow to cool to blood heat, and appl with a soft brush. When well dry, cover with plaster of Paris. Whe plaster is dry, remove cast and pour up.

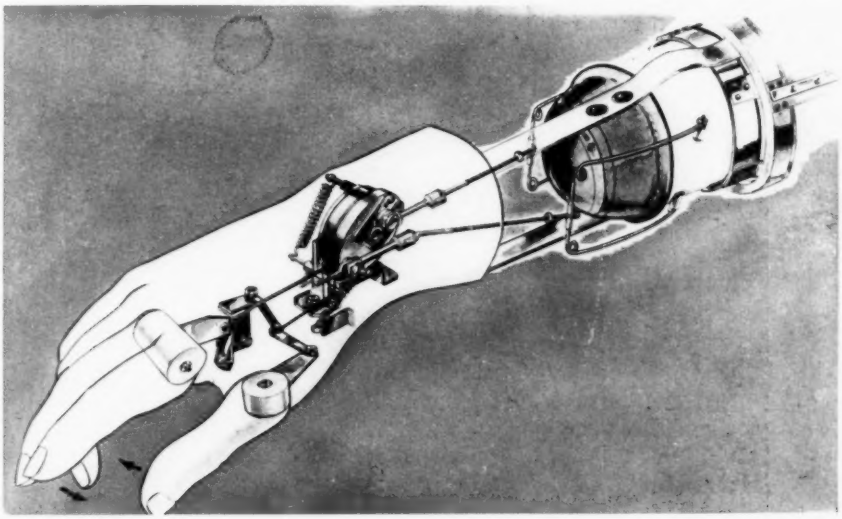

Fig. 7. Note error in technical drawing—the "toggles" cannot be in converse positions as shown. Both must be in similar positions, i.e., the digits open and close together, they cannot function separately as shown in the illustration.

The actual processing of the hollow segments of the hand casing (Fig. 9) involves a special technique of impression, waxing and counterimpression, two special interchangeable flasks being used.[1] If metal dies are required, the segments can be used as patterns.

The basic color of the hand is produced by the use of a proportionate mixture of clear and pink acrylic with the addition of yellow ochre pigment. The finesse of color, skin texture, and markings are effected later by synthetic enamel paints on the inside surface of the acrylic pieces before they are processed together. The texture appearance is improved by rendering the inside surface opaque with aluminium leaf placed over the enamel painting. The leaf in turn is again enamelled in order to protect it.

After final assembly of the hand, the esthetic effect is still further exacted by first sandpapering its surface, and then stippling all except the nail areas with an inverted cone bur. This process gives the realistic effect of cutaneous pores. If required, even further

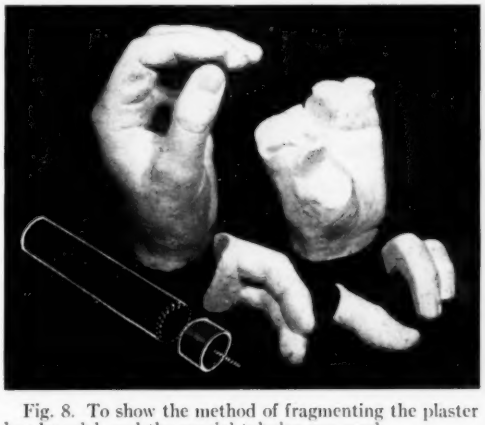

Fig. 8. To show the method of fragmenting the plaster hand model, and the special tubular saw used.

[1] *The hollow casting technique.* The technique of making hollow pieces is simple but lengthy. Each part must be made in at least two pieces. Two flasks are required, the opposing half of which must be interchangeable. Larger flasks are needed for the bigger pieces. Each fragment from the artificial stone model of the hand segment is invested in plaster to the center of its widest diameter horizontally in the bottom half of the flask. The top half is placed in position and plaster is filled in in the usual manner. When set, the halves are parted and the model of the segment is removed from the plaster impression now in the flask. Both halves of the impression are then lined with wax to the desired thickness of the hand casing. The edge of the wax in one half is cut square—that of the wax in the other half is slightly bevelled down toward the center. This bevelled edge is then built up with wax. After waxing this edge, the other half of the flask is moistened to prevent sticking, and the twin halves of the flasks are then pushed together. This procedure gives accurate registration of the edges.

Each portion is now processed separately thus—the top of the second flask is placed on the bottom half of the first containing the waxed up pattern and filled in with plaster. The other half is treated similarly. When both are processed, they should fit well, and if not must be trimmed to do so before they are in turn fused together.

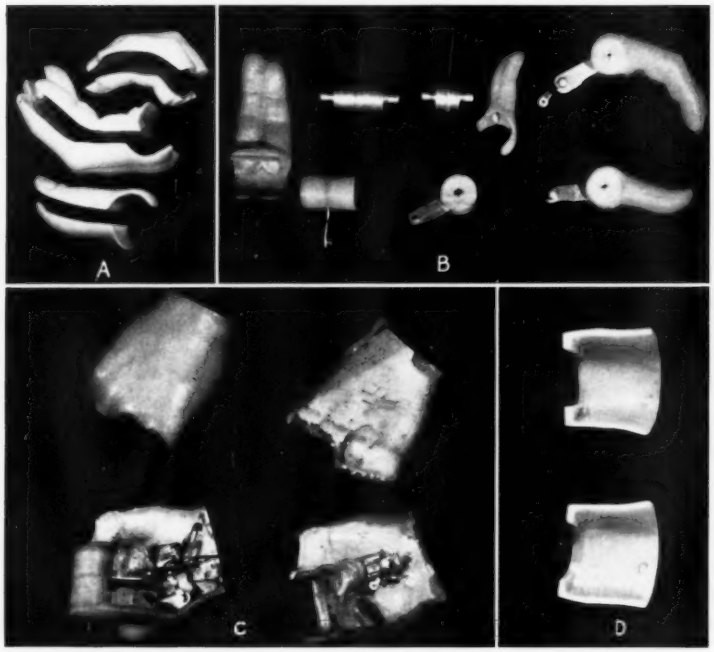

Fig. 9. To show the separate acrylic segments of the hand casing and something of their assembly: A, Segments of the finger pieces (6). B, Arrangement of assembled fingers and fitting of drums in the cut-out bases of thumb and the two fixed opposing fingers. The dural bases of the acrylic coated drums are shown. C, Front and back portions of the hand proper—2 sets, showing the fitting of the finger drum and early stages of infitting the mechanism. D, Separate halves of the wrist casing.

color can be added to the external surface by painting with an acetone solution of appropriate pigment.

A disadvantage of acrylic is its smooth, hard, slippery surface, unsuited to the handling of small objects. To offset this, the contiguous surfaces of thumb and opposing fingers are cut out with a drill and the defect made up by in-fitting cushions of polyvinyl chloride (artificial rubber). These pads are made concave on their inside, which increases the cushion effect. They are processed in place with acrylic gum.

The separate pieces of the hand casing are fused together by a thin mix of acrylic or a special gum. Volar and dorsal halves are left separate until the mechanism is in-built. The in-building is facilitated by provision in the internal structure of the shell of appropriate platforms and projections for attaching the mechanism.

The Intrinsic Mechanism

Details of the intrinsic mechanism are represented in the "exploded" diagram, Figure 10. Mild steel case hardened, duralumin and brass are all used in the mechanism, with a view always to the most effective combination of lasting strength and lightness.

The essential principle consists of a transmission of the muscle pull by a system of stirrups and transmission rods to a double toggle system of levers. One of these toggles effects movement of the thumb by its attachment to a drum in the thumb joint. The other toggle similarly effects movement of the fused index and middle fingers. Intercepting the

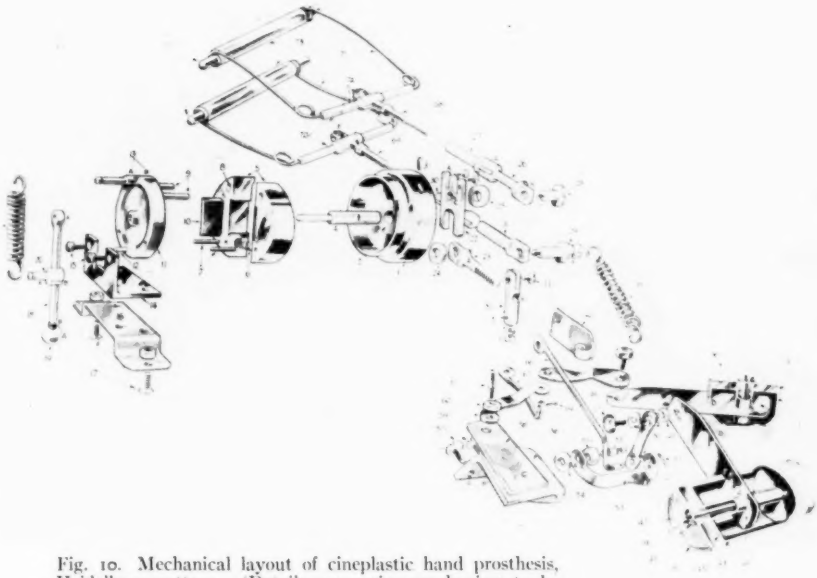

Fig. 10. Mechanical layout of cineplastic hand prosthesis, Heidelberg pattern. (Details concerning mechanism to be obtained by writing authors.)

transmission rods is a brake drum which serves a three-fold purpose: (1) it projects extensor and flexor muscle function, acting in converse ways to the common toggle system; (2) it has an equalizing effect on the difference in power between flexor and extensor muscles; (3) it acts as a locking device, so that a fixed grip can be maintained in any position without continued muscle effort.

The chief features effecting this mechanical principle are:

1. *Metal stirrups.* Each stirrup forms a spring clip with the metal core of acrylic rods which are made to fit the muscle tunnels in the stump.

2. *Connecting rods.* These are attached to the center of each stirrup and include hinges to give a universal movement. The flexor rod is attached to the lower portion of the brake drum, but its effective pull is continued by the toggle system. The extensor rod is attached to the opposite diameter of the brake drum surface.

It will be noted that by this arrangement, both flexor and extensor rods can produce their contrary effects on the common toggle system.

3. *The brake drum and locking device.* This feature essentially consists of a drum turned to shape from dural rod (Figs. 11 and 7). Into the drum are fitted friction or brake shoes which are brought into the locking position by a cam shaft operated by a lever, which passes

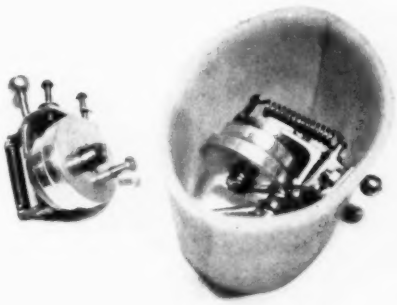

Fig. 11. The brake drum and locking device, and its location in the wrist casing.

Fig. 12. The general appearance and usefulness of the Heidelberg pattern forearm cineplastic prosthesis.

through the wrist casing. The shoes are brought firmly against the inside of the drum to act like the brakes of a car.

The operating lever is fitted with a tension spring arranged in an eccentric manner to hold the lever in either the locked or unlocked position.

On the smooth surface of the drum the connecting rod from the flexor stirrup to the toggle system is intercepted by and runs freely on a screw which is placed as near as possible to the edge of the drum. With muscle contraction to close the finger, the drum revolves with the pull of the flexor rod. Diametrically opposite on the drum, the extensor operating rod is attached by a screw to a slotted plate on the drum. This plate can be moved in or out from a central position, so altering the radius and increasing or decreasing the length of effective pull of the extensor rod. By this means, variation in the relative strength of the extensor muscle is catered for. The relatively weaker pull of the extensor muscles is also assisted by an antagonizing spring on the flexor connecting rod.

4. The finger drums. The finger drums form the mobile joints of thumb and apposing fingers. Each consists of a hollow duralumin drum with fitted ends and coated with acrylic (Fig. 9). Through the center of each drum a core of duralumin tube serves two purposes. To it is fixed the metal lever on which the toggles are attached, and it also accommodates bearings at either end in which fit stainless steel pins forming the axle of the drum.

The Accessory Fittings

The wrist portion of the assembled hand is attached by duralumin bars (1) to a leather

and/or metal cup[1] which must be made for each case to fit accurately to the end of the amputation stump. It acts as a counter pressure point for the effective pull of the muscles through the intrinsic mechanism. (2) The bars further extend to a second attachment on one ring of a ball race situated at a level below the elbow region.

By the ball race, some pronation and supination movements are obtained. The other ring of the ball race is attached by elbow hinges to a well fitting but not tight molded armcuff. The cuff is trimmed and arranged so as not to embarrass the biceps muscle. The usual accessory body straps are attached as required.

THE MODIFIED HEIDELBERG PROSTHESIS FOR A SINGLE TUBE CINEPLASTY

In these cases, only the flexor muscles are used. All parts of the prosthesis pertinent to the extensor muscles are dispensed with. The opening of the grip is effected by a spring antagonizing the flexor rod in a position as indicated in Fig. 7.

Considered advantages of the Heidelberg prosthesis are:

1. *A high standard of esthetic appearance.* All of the amputees so far supplied with these arms continue to wear them, and, when carefully questioned, one of the chief reasons is that they "look well" (Fig. 12). To personnel in a sedentary type business occupation, as most of our small series are, this is a good reason. Acrylic is not the ideal medium, but it does set a high standard in this regard for future materials and improvements.

2. *The mechanical lever system* is simple and efficient, and effects a good useful range of strong finger movement.

3. *The locking device* permits of the prosthesis being used in a passive manner. Long continuous gripping of objects—e.g. pen or knife—can be effected without continued muscle action. Metal clips on the common utensils are required to stabilize the grip by the nonresilient acrylic (Fig. 12).

4. *Total weight* of recently completed prostheses with all accessory fittings is 1 pound 8 ounces. This is much lighter than the dress arm normally supplied.

5. *The hand is durable and serviceable* despite a highly esthetic and somewhat fragile appearance. These hands have given little trouble in our small series to personnel outside the manual laborer class.

The chief disadvantage of the prosthesis is the limited effective range of the finger movement (only 1⅜ inch). This is dictated by the space available for the lever system. We consider this may be improved by modifying the lever system and using a "knuckle joint" or a "sliding plane" in the thumb system, if not in the opposing finger system as well.

RESULTS

Our experience of cineplastic amputations is confined to the forearm and that limited to 12 cases. It is recognized that only by a large case series carefully controlled over a long period could any finite conclusion be made, but in view of the times and our early encouragement, we consider such an interim statement indicated, immature though it is. All patients fitted with a cineplastic prosthesis continue to wear them to date, and remain enthusiastic. That must be the ultimate judgment of their value. Kessler in America states that 60 per cent of the 264 cases continue routine use of their prostheses. Jottkowitz quotes 40 per cent of his 728 cases, while in the Saurbruch clinic, 60 per cent of 304 cases are recorded as satisfied.

Careful preselection of cases must be made the prime factor for the success of any cineplastic procedure. No procedure would be more doomed to failure by any haphazard or mass application. All types of upper arm prostheses have their limitations—a cineplastic is one of them. Some individuals may be of such mental caliber or vocation that they would be better without any prosthesis at all. Some may be better suited to a bucket with attachments; others may require only a cosmetic substitute, or may need and derive great benefit and help from a cineplastic prosthesis.

A cineplastic prosthesis is not something automatic, but something of which the wearer must learn the true use himself. Cine-

[1] In recent models, these cups have been made of reinforced acrylic, as shown in Figure 6. Polyvinyl chloride may be a still better medium for this purpose.

plasty is no proposition for a flabby personality. In the preselection of cases, the chief considerations are:

The individual, his attitude, and will. He must be fully informed of the implications of the procedure, and its limitations. The early expectations of upper limb amputees are often too great. The salesmanship of a manufacturer or town gossip may contribute to this mistake, which should never be allowed to continue for any lack of careful explanation. Sad realization of the gross inadequacy of an artificial arm when supplied as compared with that of his hopes, has—in the past—often led not only to its rejection, but to a deep-rooted prejudice for any appliance. An amputee can always escape in an unfortunate sense of honor to have lost an arm and to show it.

Type of work or vocation. Forearm cineplasty is most satisfactory for a sedentary type occupation. It is of little use to the manual laborer for his work, but even he may value it in sedentary life and leisure. It is not incompatible with the alternate use of other limbs and appliances on the same stump.

The amputation stump. Prerequisites in this regard have been set out. There must be adequate length of forearm to permit a satisfactory cineplastic operation. We have had no experience with upper arm cineplasty, but the prosthetic technical difficulties associated with it must range against its relative value.

Site of amputation relative to dexterity. All right-handed amputees or their left-handed counterparts who are missing on the same side, would be better considered for a cineplasty than those missing on the opposite side. The bilateral amputee would seem always the strongest indication for cineplasty.

CONCLUSION

We believe with modern progress both in plastic operations and a better order of prosthesis, that cineplastic procedures as described must have a wider application than we know of at present.

It is hoped that our experiments and results might stimulate trial on a larger scale than our numbers, time and facilities might permit.

There are many ex-service personnel who have lost their right hands in the service of their country and their fellows, and their least dessert is the pan-ultimate that modern science and surgery can contribute to their re-construction.

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THE EFFECT OF PULMONARY RESUSCITATIVE PROCEDURES UPON THE CIRCULATION AS DEMONSTRATED BY THE USE OF RADIOACTIVE SODIUM

SAMUEL A. THOMPSON, M.D., F.A.C.S., EDITH H. QUIMBY, Sc.D., and BEVERLY C. SMITH, M.D., F.A.C.S., New York, New York

IN asphyxia, the object of all resuscitative procedures is to produce an adequate pulmonary ventilation. Negovski and his co-workers have recently added to pulmonary ventilation, the intravascular injection of oxygenated blood and glucose in their efforts at "revival" (1). The majority of investigations in resuscitation have dealt with the degree and efficiency of the ventilation produced by the various methods. Such ventilation occurs as a result of: (a) inflation of the lungs and return to the starting point; (b) deflation of the lungs and return to the starting point; (c) alternate inflation and deflation of the lungs. The procedures are classified as manual or mechanical, and are of various degrees of efficiency. A measured and constant amount of ventilation can be produced only by mechanical means, controlled by either a constant volume or a constant pressure. Large volumes or excessive pressures may cause alveolar rupture and for this reason controlled pressures are safer than controlled volumes. Only resuscitators with a controlled pressure should be used. No control or constancy exists with any manual method.

Pulmonary ventilation alone is insufficient to produce resuscitation, particularly when circulation has stopped. Oxygenated blood in the lungs is of no value unless it can be moved out and transported to the vital centers of the nervous system. Such a movement of the blood does take place in certain methods of resuscitation, varying in rate and volume with the method used.

From the Department of Thoracic Surgery, New York Medical College, Flower-Fifth Avenue Hospital, and from the Departments of Radiology and Surgery, College of Physicians and Surgeons of Columbia University, with the aid of a grant from the Lilla Babbitt Hyde Foundation.

Very little emphasis has been placed upon this aspect of resuscitative procedures, and no definite study appears to have been made of it. Actually, until recently there has been no satisfactory way of demonstrating whether or not any given procedure could produce an actual movement of the blood column. The purpose of the present paper is to describe a method for determining the relative effects of various types of pulmonary resuscitation upon the circulation, and to give some experimental results obtained thereby.

This method consists essentially in introducing a tracer substance into the vascular system of an animal immediately following death by asphyxiation and recording any movement of this substance during the application of the resuscitative procedure. The tracers which have been employed are radioactive sodium, fluorescence, and oxygen. This concerns the use of radioactive sodium only.

The use of artificially radioactive isotopes as tracers has become rather familiar in the field of experimental medicine in recent years. Sodium, used in the present study, is made radioactive by deuteron bombardment in the cyclotron and then emits penetrating radiations which can be detected by means of a Geiger-Mueller counter. A small amount of this material, in normal saline, injected into the circulatory system of the living animal, is rapidly carried throughout the body; its presence in any region can be demonstrated by placing the counter against the surface of the body at that part (2). In an animal whose circulation has ceased, such distribution could not occur. A counter placed over the body at a place distant from the site of injection would register only a small background count, due

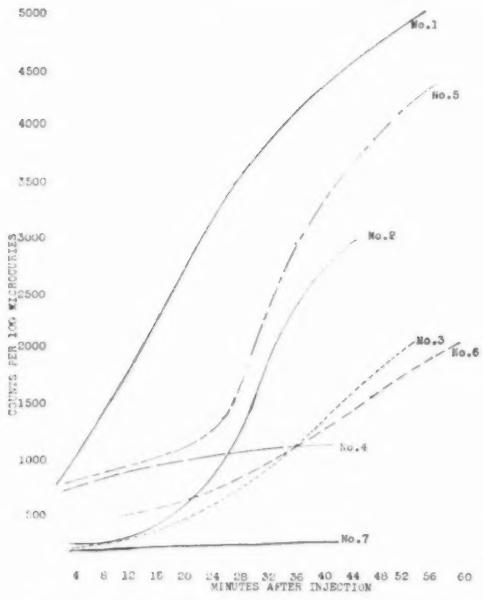

Chart 1. *No. 1*, Heparin, intravenous sodium, double action resuscitator; *No. 2*, heparin, intravenous sodium, double action resuscitator; *No. 3*, heparin, intra-arterial sodium, double action resuscitator; *No. 4*, no heparin, intravenous sodium, double action resuscitator; *No. 5*, heparin, intravenous sodium, suction only; *No. 6*, heparin, intravenous sodium, pressure only; *No. 7*, control, heparin, intravenous sodium, no resuscitator.

to the presence of the sodium in the distant region. As long as the radioactive material remained essentially at this position, the count would remain the same. If, however, any movement of the blood in the veins and arteries could be brought about by a resuscitative procedure, the radioactive sodium would also be moved, and any appreciable shift toward the counter would be demonstrated by an increase in the counting rate.

TECHNIQUE

Dogs 14 to 20 kilograms in weight were used, the following procedure being carried out: The animal was anesthetized with intravenous or intraperitoneal nembutal. An endotracheal tube with occlusion cuff was then inserted and the cuff inflated to make the tube leak-proof. To prevent intravascular clotting of the blood, 2 to 5 cubic centimeters of heparin were injected intravenously. Approximately 5 minutes after the injection of heparin the endotracheal tube was completely clamped off, and the animal allowed to succumb to obstructive asphyxia. Cardiac cessation and death according to clinical evidence took place about 8 to 10 minutes after the tube was clamped. However, in order to insure complete death with no subsequent cardiac activity, the tube remained clamped for an additional 20 to 30 minutes. The animal was placed on an inclined plane, with the head elevated about 20 degrees, to counteract any possible effect of gravity in causing diffusion of the tracer substance toward the heart.

At the end of this time about 2 cubic centimeters of normal saline, containing 50 to 60 microcuries of radioactive sodium were injected into a femoral vein or artery. The Geiger-Mueller counter was placed against the neck of the dog, in proximity to the carotid artery, and the resuscitative procedure started and carried on for 40 to 60 minutes.[1] During this period, starting at the instant of injection of the radiosodium, the counts per minute registered by the counter against the neck were recorded. These counts were plotted on a curve showing any change in counting rate with time after the start of resuscitation (Chart 1).

After the mechanical procedure had been carried on for this period, and the effect was evident, the resuscitator and counting were stopped and 5 cubic centimeter blood samples taken from the femoral vein and artery on the opposite side from that injected, the right and left side of the heart, the jugular vein, and one carotid artery. Careful measurements were made of the amount of radioactive sodium contained per cubic centimeter of each of these samples (Tables I and II).

Experiments were carried out with various possible combinations of conditions:

Intravenous sodium with (a) alternate inflation and deflation of the lungs; (b) inflation and release; (c) deflation and release.

Intra-arterial sodium with (a) alternate inflation and deflation.

[1]The resuscitators used positive pressure of plus 14 millimeters of mercury, negative pressure of minus 9 millimeters of mercury. The rate was set at 16 to 20 per minute.

TABLE I.—RADIOSODIUM CONTENT OF DOGS' BLOODS

No. of experiment	Weight of dog kgm.	Type of resuscitative procedure and site of injection	Assumed blood volume c. c. (1/7 weight)	Microcuries radiosodium injected	Microcuries per c. c. if entire dose were uniformly distributed*
1	19.5	Intravenous sodium Heparin Double action respirator	2790	50	0.018
2	18.7	Intravenous sodium Heparin Double action respirator	2670	50	0.019
3	16.1	Intra-arterial sodium Heparin Double action respirator	2300	50	0.022
4	20.8	Intravenous sodium No heparin Double action respirator	2970	60	0.020
5	16.5	Intravenous sodium Heparin Suction only	2360	60	0.025
6	16.9	Intravenous sodium Heparin Pressure only	2410	50	0.021
7	13.8	Intravenous sodium Heparin No respirator	1970	50	0.025

*Actually some of the sodium would have passed into the extravascular fluid, so this value is probably somewhat high.

Controls, with intravenous sodium with (a) heparin with no resuscitative procedure; (b) alternate inflation and deflation with no heparin.

RESULTS AND DISCUSSION

A heparinized animal recently succumbed to obstructive asphyxia provides an ideal subject for observing the effect of any given resuscitative procedure upon the circulation, provided a tracer can be introduced into the blood so that its movement can be followed. Any such movement would depend on the fact that the mechanical inflation and deflation of the lungs produce a regular filling and emptying of the pulmonary capillaries and a regular alternation in pressure upon the heart and great vessels of the mediastinum. Since the valves of the heart and veins prevent a back flow of blood, any movement of the circulation must be in one direction, and if of sufficient rate and volume would complete the circuit from left heart to artery, to capillary, to vein to right heart, to lungs, and thence back to left heart again. Such movement of blood containing radioactive sodium could be detected by the Geiger-Mueller counter, its rate recorded, and some idea obtained of its volume.

TABLE II.—RADIOSODIUM CONTENT OF BLOOD SAMPLES, IN PERCENTAGE OF CONTENT FOR UNIFORM MIXING OF ENTIRE ADMINISTERED AMOUNT

No. of Experiment	Opposite femoral artery	Opposite femoral vein	Carotid artery	Jugular vein	Right auricular appendix	Left auricular appendix
1	17	28	22	22	22	33
2	63	42	63	21	37	58
3	59	0	50	14	59	59
4*						
5	16	80	16	150	160	12
6	38	210	0	0	33	33
7	Trace	Trace	0	0	0	0

*No samples could be taken from this dog having no heparin.

The experimental data for 7 dogs are shown in Chart 1. Animal 7, the control with no resuscitative procedure but with heparin and radioactive sodium, showed no increase in count at the neck during 40 minutes. This demonstrates that there is no significant motion of the sodium due to diffusion or any other process occurring when no resuscitator is employed. In animal 4, the control having no heparin, the count rose only very slightly. On postmortem examination a large clot was found in the abdominal inferior vena cava, which would have prevented any further passage of radioactive sodium beyond this point. With all of the other animals, after a short period the count began to increase, and continued to rise as long as it was followed, up to an hour. In all except animal 2, there was a delay of 15 to 20 minutes before definite change was evident; this one animal showed an immediate rise and went much higher than any other. The reason for this is not evident; there seemed to be no doubt that the dog was dead, although an extremely weak heart action would account for the finding.

With the exception of animals 1 and 2, each one was subjected to a different procedure from all the others, so that there is no data as to possible variations among animals treated in any one particular manner. Hence it is not possible to put much stress on the numerical differences in the results. However, the two dogs in which alternate inflation and deflation were employed (animals 1 and 2) and the one having deflation and release (animal 5) showed values definitely higher than the others. The one having inflation and release (animal 6) came up more slowly, as did the one in which the injection was intra-arterial (animal 3). This latter was to be expected, since the material would have to be moved first through the capillaries and then into the veins before it could start toward the heart.

The radiosodium contents of the blood specimens from the various dogs are given in Table I, with other pertinent data. It is assumed that the blood is 7 per cent of the body weight, and microcuries per cubic centimeter are calculated for uniform distribution throughout the circulatory system. This amount is what would be expected in a living dog, when mixing through the blood was completed, before diffusion into the extravascular fluid had proceeded to any significant degree. In none of the asphyxiated dogs was this distribution approached.

Certain suggestions may be advanced to explain the results in the various animals, but it must be recognized that these are tentative and could be confirmed only by repeating each test on several dogs of essentially the same weight. For instance, in animal 3, having intra-arterial sodium, apparently the procedure was not carried on long enough for the material to travel through the capillaries of the injected leg to the veins, to the heart, to the artery of the opposite leg, and through the capillary system of the opposite leg to the vein, for no active material was found at that site. Similarly it was low in the jugular vein. However, the variations in values in all the examinations indicate that the mixing of the radiosodium in the blood is far from uniform, as would be expected with this type of forced circulation. The actual radiosodium contents of the blood samples may not have much significance. The important thing is that grossly, with the counter, general movement in the circulation can be observed.

From these experiments it is quite evident that in a dead animal the mechanical inflation or deflation of the lungs or a combination of both produces a movement of the blood of sufficient magnitude to circulate it over the entire body, in a continuous direction from vein to heart, to lungs, to heart, to artery, to capillary, and back to vein again. While both the rate and the volume of this circulation are well below that in the living animal, it is, nevertheless, definite. Whether it is a result of the alternate filling and emptying of the pulmonary capillaries or of alternation in pressure upon the heart and great vessels, or a combination of both, is not yet determined (3).

That it is possible by mechanical means to circulate the blood in an animal whose heart has stopped beating would seem to have considerable clinical value. In order for the blood to be circulated it must remain fluid. Intravascular clotting takes place soon after death, and when this occurs the possibility of recov-

ery is terminated. Therefore the use of heparin intravenously as an active part of resuscitation is indicated. If, in resuscitation, heparin is given intravenously before the heart has stopped beating, thus preventing clotting, the time of possible revival is prolonged. Since the greatest amount of circulatory movement was found with alternating positive inflation and negative deflation of the lungs, this should be the method of choice. This can be done only by mechanical means; it is therefore evident that mechanical double action respirators are of the greatest value.

Because of the small number of experiments, no definite numerical conclusions can be drawn from these results. However, movement of the blood in a dead heparinized animal has definitely been shown to occur under the action of mechanical respirators. The results have been qualitatively corroborated by other experiments (to be reported later) in which fluorescence and oxygen have been used as tracer substances. Quantitative results are more readily obtained by use of a radioactive tracer.

SUMMARY AND CONCLUSIONS

A method of determining the effect of pulmonary resuscitative procedures on the circulation by the use of radioactive sodium has been described. By this method it has been possible to demonstrate that alternate mechanical inflation and deflation of the lungs, or either operation alone, produce a movement of the blood within the vascular system. This movement is sufficient in the dead but heparinized animal to circulate some of the blood throughout the entire body. Mechanical resuscitators, using alternating positive and negative pressures, produce the greatest circulation. As soon as postmortem clotting occurs, little or no motion of the blood can be brought about by resuscitative procedures. When intravenous heparin is used to prevent this clotting, the period during which blood can be moved is greatly prolonged. For this reason the use of intravenous heparin seems indicated in resuscitation, as a definite means of prolonging the possible recovery time of the asphyxiated patient.

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CANCELLOUS BONE GRAFTS FOR INFECTED BONE DEFECTS

A Single Stage Procedure

Wing Commander HERBERT M. COLEMAN, M.D., F.R.C.S. (Ed.), Major JAMES E. BATEMAN, M.D., GORDON M. DALE, M.D., and Captain DONALD E. STARR, M.D.

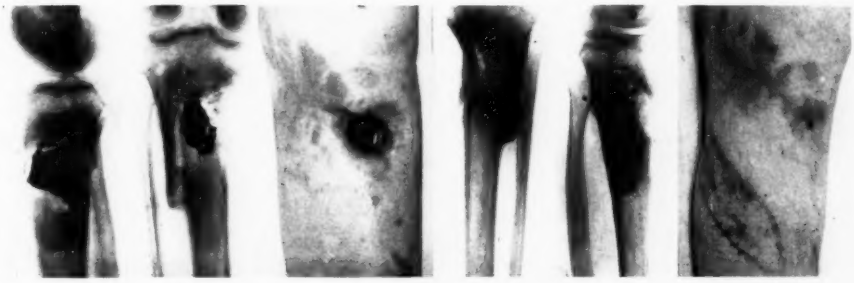
THE skillful surgery of World War II, with the help of plasma, penicillin, and sulfa therapy has saved many lives and limbs which would otherwise have been lost. The reconstructive surgeon is subsequently faced with many difficult problems in the restoration of a useful limb. Large bone defects with scarring of the overlying tissues are frequently encountered after compound fractures or gunshot wounds. In cases in which the wound has never been infected or has been healed for several months, the problem is relatively simple and can be handled by one of the common methods of bone grafting. In those cases in which the bone defect has an associated chronic low-grade infection with sequestra and sinus formation, function must be restored quickly before infection and immobilization give rise to such disuse changes as stiff joints, atrophy, and fibrosis of muscles, together with circulatory changes.

In January, 1944, Dickson stated that, "a surgical bone graft should not be attempted in the presence of active infection even if low grade. An occasional success does not justify the risk of almost certain failure to be anticipated." "Placing a bone graft in an infected area, therefore, must be characterized as surgically unsound and a violation of the principles of bone graft surgery." In the series under review over the past 14 months, 52 infected bone defects have been cleaned out, filled with cancellous chip grafts and the wounds closed without drainage. This procedure, in direct violation of the principles here enumerated, has yielded results which are extremely gratifying. In only 4 cases has the result been unsuccessful with continued infection, resulting in sequestration of the grafts or further sequestrum formation in the grafted bone. The remaining 48, or 92 per cent, are healed with the bone defects obliterated.

In the summer of 1944 several patients were admitted with sinuses leading down to large cavities in the upper end of the tibia (Figs. 1, a, b, c; 3, a, b, c; 12, a, b, c, d.). The defects were such that they could not be dealt with in the usual manner by saucerization or filling with muscle grafts. This type of osteomyelitis had been a problem after the last war, and many of them eventually came to amputation (Fig. 2). Visits to other orthopedic centers found these patients being treated from month to month with courses of penicillin or sulfa drugs without effect.

In view of good results following sequestrectomy with closure of wounds under penicillin and the successful use of chip grafts in the mandible by the plastic surgeons in the presence of infection, it was our opinion that cancellous grafts could be used in other bones as well. Mowlem (6, 7) has reported 85 cancellous chip grafts. Eleven of these were done in the presence of infection, 2 in the tibia and the rest in the mandible and skull. He considers fragmentation of the graft provides a greater surface through which transplanted bone cells become accessible, first to serum and then to newly formed capillaries, thus making their survival more certain. We have confirmed his observation that cancellous bone has an unusual degree of resistance to infection. Whether the grafts die and are replaced or go on living, as Mowlem states, is difficult to say from x-ray evidence. Whatever the process may be, the fragmentation results in rapid new bone formation. We have noted the new cortex formation which he describes (Fig. 13e). In 5 instances, ununited

From the Combined Services Orthopaedic Unit Christie Street Hospital, Toronto, Ontario.



a b c d e f

Fig. 1.

Fig. 1. Case 3, H. W. a, b, c, A large defect in the upper tibia filled with lipiodol. From this cavity Staphylococcus aureus and Bacillus proteus were cultured. At one sitting the cavity was cleaned out and filled with cancellous bone chips. d, e, f, The same case 4 months later with the cavity consolidated and the wound healed. The patient has 90 degrees of knee movement. The apparent sinus in f is only a retraction of the scar at this point.

Fig. 2. Three examples of traumatic osteomyelitis with cavity formation which came to amputation after World War I.

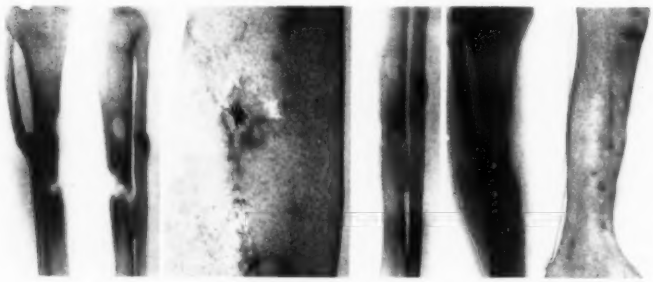
Fig. 3. Case 6, J. C. Gunshot wound of tibia. a, b, c, Show the condition on admission. The sinus was infected with hemolytic Staphylococcus aureus, and Aerobacter aerogenes. Note the ununited fracture of tibia, and the sequestra. The fracture was united in 2 months. f, The condition of the wound at the first change of plaster, d, e, g, Final result.

Fig. 2.

a b c d e f g

Fig. 3.

linear fractures were present in relation to a defect and united rapidly after grafting. Two of these in the tibia were united in 2 months (Figs. 3, a, b, c, d, e, f, g). In two instances complete defects were present. One of these was solid enough for weight bearing after 7½ months, and the patient has been on full activities for 5 months. The other case (Fig. 4, a, b, c, d) is solid at 6 months with obliteration of the defect.



a b c d

Fig. 4. Case 30. V. G. A complete defect in the tibia following a compound fracture. The sinus shown in b, was infected with Staphylococcus aureus and Bacillus proteus. Sequestra were present in the defect. The tibia was solid 6 months after sequestrectomy with cancellous bone grafting, as shown in c and d.

TECHNIQUE OF OPERATION

Preoperative and postoperative care. The patient is started on 20,000 units of penicillin intramuscularly every 3 hours, 2 days before operation. This is continued postoperatively until his temperature has remained normal from 2 to 5 days. At operation a pneumatic tourniquet is used to ensure a dry field. This is essential for complete sequestrectomy. Any sinus is injected with methylene blue so that no infected tissue will be left behind. All scar tissue, granulation tissue, and sequestra are removed. The cavity is excised with an osteotome or curetted down to healthy bleeding bone. Where feasible, a block resection of the bone defect is done. The wound is washed out with saline, and penicillin sulfathiazole powder, 100,000 units to 20 grams, is sprinkled liberally during the operation to ensure that all exposed tissues are protected. The periosteum is stripped as little as possible.

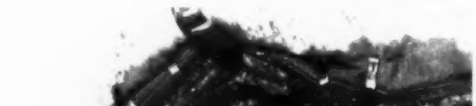


Fig. 5. The anterior iliac crest is here exposed. The arrow points to the wedge of cancellous bone ready to be lifted out.

The grafts are taken from the anterior portion of the iliac crest by an assistant and the two fields are kept separate. Both iliac crests are prepared, as the full extent of the cavity cannot be determined from the x-ray picture and is usually much larger than expected. The posterior iliac crest has also been used. The crest is exposed with as little stripping of periosteum and muscles as possible. The contour of the ilium is maintained. A trap door of cortical bone with attached periosteum is raised from the crest of the ilium. A wedge of cancellous bone (Fig. 5) can then be cut and further bone obtained with a curette. The wedge of cancellous bone is shaved with a sharp osteotome into thin chip grafts. *All* cortical bone is removed from the cancellous bone. This is essential as cortical bone has less resistance to infection (Figure 11, a, b, c) demonstrates this point. A previous chip graft was done in England using cortical and cancellous bone from the tibia. The graft was unsuccessful and the cortical sequestra can be seen in the roentgenogram (Fig. 6, a). Cancellous chip grafting was successful (Fig. 6, b and c).

The chips are mixed with the penicillin sulfathiazole powder and packed loosely into the cavity. The bone edges are bevelled and overlapped with chips to increase the surface in contact. One of us (J. E. B.) fills the cavity

a b

Fig. 6.

a b

Fig. 7.

Fig. 6. F. D. a, A defect of the upper tibia involving the knee joint, infected with Bacillus proteus. A one stage sequestrectomy and arthrodesis with insertion of cancellous bone grafts was done. b, The knee was soundly arthrodesed 4 months later.

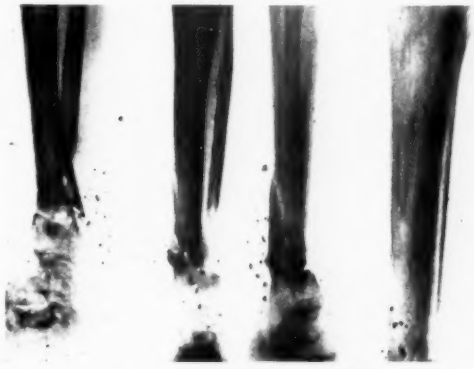
Fig. 7. Case 2, J. Mc. a, An abscess of the upper tibia from a blood-borne infection in childhood. A sinus was present infected with Staphylococcus aureus. b, Three months after filling the defect with cancellous bone. There has been no recurrence of infection 14 months later.

with chips and penicillin powder held together with coagulated autogeneous plasma. One to 2 cubic centimeters of .02 per cent sterile agar is added as a coagulant. This produces a vehicle of jelly-like consistency fixing the sulfathiazole and penicillin to the fragments. The time of absorption of the penicillin and sulfathiazole is prolonged and the plasma produces more concentrated nourishment for the grafts than blood clot. The skin defect is then closed. If more than a simple plastic procedure is necessary, the operation is completed by a plastic surgeon. The limb is enclosed in a plaster-of-Paris cast, which is not changed for 3 weeks. Soft tissue immobilization is important for healing and the limb must be immobilized until the grafts are consolidated.

This report is necessarily a preliminary one, as the series covers just over a year and many of the cases have been done in the past few months. The final fate of the grafts will have to be evaluated, but to date they have formed good bone with no evidence of absorption with use.

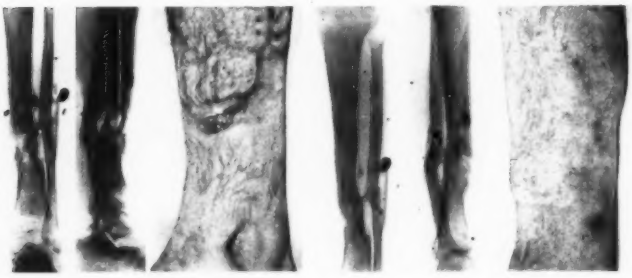
Site of defect. The tibia was involved in 29 cases, the femur in 12, the os calcis in 3, the humerus in 6, the carpus in 2.

In all 52 cases infection was present at the time of operation. Preliminary sequestrectomy was done by us in 6 of these, and many had had a previous sequestrectomy which had not been successful, as sequestra still remained. Three plates, a screw, wire, and numerous foreign bodies were also removed. Sequestrectomy was not done as a separate operation unless the patient was being anesthetized for a preliminary plastic procedure and the defect was readily accessible. In bones clothed by muscle, the extra opera-



a b

Fig. 8. Case 28, P. G. A compound fracture of tibia infected with Staphylococcus aureus, diphtheroid and Bacillus proteus. A caterpillar graft was completely lost, but did not affect the take of the cancellous bone grafts as shown in, b.



a b c d

Fig. 9. Case 22, G. M. a, b, the preoperative condition. c, d, 4 months after sequestrectomy and cancellous bone grafts. The skin wound was closed by a rotation flap.

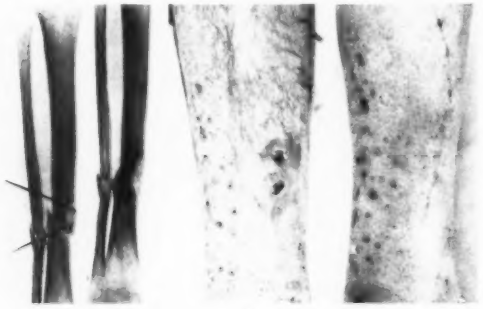
tion will increase muscle fibrosis. In the tibia it is likely to increase the skin defect and make subsequent wound closure more difficult. We do not consider that there is anything to be gained by a preliminary sequestrectomy, as the granulating cavity must be curetted again before insertion of the cancellous grafts. Sequestrectomy with preliminary split skin grafting of the cavity which has recently been described (4, 5) would appear to be an unnecessary procedure, with far from assurance of a complete take of the skin grafts and no assurance of the eradication of the infection in the time which elapses before the final bone graft is carried out. Sterilization of the wound is obtained by the complete excision of all infected scar, granulation tissue and diseased bone with the aid of penicillin and sulfathiazole. Any failure in the take of the split skin graft leaves a portal of entry for further infection.

CAUSE OF INJURY AND SOURCE OF INFECTION

The cause of injury and source of infection were as follows:

1. Gunshot wounds involving bone	45
2. Compound fractures	3
3. Bone infection following open reduction of simple fractures	2
4. Bone abscesses from childhood osteomyelitis	2

The 2 cases of bone abscess from a blood-borne infection in childhood had had recurrent acute attacks, and both were infected with Staphylococcus aureus. Healing occurred without

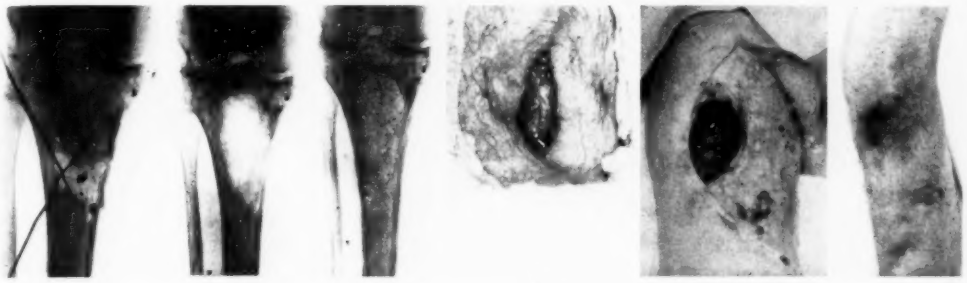


a b c

Fig. 10. Case 25, W. W. Infection following open reduction of a fractured tibia. a, b, Show the sinuses with sequestra formation. a, c, Tibia united and the wound healed, 4 months after sequestrectomy with cancellous bone grafts.

a b c

Fig. 11. Case 5, R. C. Gunshot wound of tibia. Bo chips from tibia were inserted in the defect in Englan The cortical bone has sequestrated, as shown in a. I was admitted with a sinus from which Staphylococc aureus and pyocaneus were cultured. b, The defect af cancellous bone grafts from the iliac crest. c, The wou healed by primary intention.



a b c d e f

Fig. 12. Case 9, A. M. Gunshot wound of the left tibia with a large sinus and sequestra, a, d, b, e. The extent of the cavity after sequestrectomy took place. c, f, Final consolidation of the cavity with the wound healed. There was a partial loss of the split skin graft over the donor area.

i cident, and there were no symptoms, and the cavities were obliterated (Fig. 7, a, b).

BACTERIOLOGY

In 21 instances, the infection was a mixed one. Penicillin was given to all patients routinely, despite the presence of penicillin-resistant organisms. Bacteriology in 10 cases was incomplete—either no growth was reported or no report was found. The organisms in their frequencies were:

Staphylococcus aureus	17
Bacillus proteus	11
Diphtheroid bacillus	7
Pyocyaneus (Pseudomonas)	7
Hemolytic streptococcus	3
Nonhemolytic streptococcus	3
Escherichia	3
Staphylococcus albus	2
Aerobacter aerogenes	2
Clostridium	2
Alcaligenes	1
Bacillus coli	1

In the 4 failures the organisms found were: In case 14, the Staphylococcus aureus (resistant to 30 units penicillin per 100 c.c.); in case 19 the Bacillus proteus and a clostridium; in case 29 the Staphylococcus aureus, aerobacter, pseudomonas, and Bacillus proteus; in case 51 the Bacillus proteus.

In these 4 cases, organisms resistant to penicillin were present and were undoubtedly a factor in the failure. In 3 of these further sequestra have been demonstrated, probably due to the interference with the blood supply of relatively avascular bone, plus continuing infection. The other failure was in a cavity surrounded by very sclerotic bone. The chip

a b c d e

Fig. 13. Case 10, A. H. Compound fracture of tibia by a V-2 bomb. Patient was admitted with a sinus and sequestra, as shown in a, b, d. The wound healed at the first change of plaster. c, The cavity obliterated 3 months after sequestrectomy with cancellous bone grafting. e, Is a roentgenogram 11 months after cancellous bone grafts. Note the excellent quality of the bone with a new cortex formation.

grafts were later removed and had sequestrated with no evidence of osteogenesis. Poor blood supply to the grafts plus penicillin-resistant organisms resulted in failure. No virulent flare-up of infection has resulted from operation in any of the 52 patients.

WOUND CLOSURE AND IMMEDIATE RESULTS

Extensive scarring and sinus formation were present in almost every case. This necessitated some form of plastic closure of the wound in 30 instances. The plastic procedures included local mobilization of the skin edges, rotation flaps, double-ended local pedicles, 2 abdominal pedicles, and 1 caterpillar flap. In some instances the skin was mobilized completely around the extremity over a wide area. In 33 cases the wounds were perfectly healed at the first change of plaster. Of the remaining 19 all are healed except 2.

The causes of failure of the wounds to be completely healed at the first change of plaster were: persistent sinus to bone in 5, loss of flap or a portion in 3, superficial necrosis of skin edges due to tension in 8, hematoma in 2, and stitch abscess in 1.

The 8 cases in which the superficial dry necrosis occurred could probably have been avoided with more careful closure. These all healed with no infection and minimum scarring. The loss of a flap or a portion did not affect the underlying cancellous grafts. In 1 case in which a complete caterpillar graft was lost (Fig. 8, a, b) the remarkable viability of cancellous chip grafts was demonstrated. None was lost and the cavity has consolidated. To date there has been no reopening of any wound or flare-up of osteomyelitis after healing.

In an additional series of 5 cases in which infected bone defects involved joints (Fig. 6, a, b), the same routine has been carried out. All of these are healed; 3 are firmly arthrodesed and the other 2 have been done too recently to expect arthrodesis.

SUMMARY AND CONCLUSIONS

1. In 52 infected bone defects cancellous chip grafts have been inserted after sequestrectomy and the wound closed, with success in 92 per cent.

2. The method is applicable to traumatic osteomyelitis and some cases in which the infection has been blood-borne.

3. No virulent infections have resulted and there has been no flare-up of infection after healing, for periods up to 14 months.

4. In a small series in which traumatic osteomyelitis involved joints, chip grafts have been used after sequestrectomy with healing and satisfactory fusion.

5. Successful chip grafting in the presence of infection depends upon (a) complete sequestrectomy and removal of all infected tissue; (b) an adequate vascular bed for the grafts which must have all cortex removed; (c) no dead spaces; (d) penicillin, systemically and locally, with sulfatherapy, if indicated; (e) full thickness skin to close any skin defect; (f) plaster immobilization (for soft tissue healing and until the bone is consolidated).

6. The one stage method for obliterating infected bone defects saves months of hospital treatment and restores function before disuse changes become irremediable.

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OUTLET PELVIMETRY

A Commentary, and the Presentation of a Pelvimeter for Measuring the "Symphysis and Sacral Biparietal Distance"

HERBERT THOMS, M.D., New Haven, Connecticut

THE measurement of pelvic outlet diameters has always presented certain difficulties, whether the attempt to determine these dimensions has been by manual or roentgenological means. In the former case, because of a lack of definite palpable end points for the intertuberal or transverse diameter, the estimation of this dimension may be quite variable in the same individual even when measured by experienced observers. Roentgenologic methods for depicting the pubic arch have not proved very satisfactory because of distortion difficulties. Lateral pelvic views, nevertheless, are very useful in determining anteroposterior diameters and relationships. However, important morphological data can be obtained by either method, manual methods being particularly valuable in determining the shape and general size of the pubic arch.

The pelvic outlet in relation to labor presents a mechanism which it is useful to consider. With a normally shaped pubic arch with adequate capacity the head extends with the occiput in close contact with the subpubic angle. The arc described by the extending sinciput is minimal under these circumstances and the likelihood of perineal damage is also minimal (Figs. 3 and 4).

However, when the subpubic angle is narrow and the capacity of the arch is thereby lessened, the head as a whole is forced backward, the biparietal diameter engaging the ischiopubic rami; the arc of the extending sinciput is lengthened, and the liability of soft tissue damage thereby increased. It is obvious, therefore, from the mechanics of

From the Department of Obstetrics and Gynecology, Yale University School of Medicine.

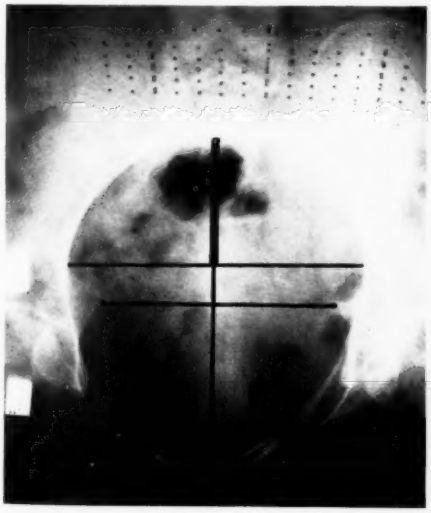


Fig. 1. Roentgenogram of pelvic inlet diameters as shown in Figure 8. (Correction scale at top.)

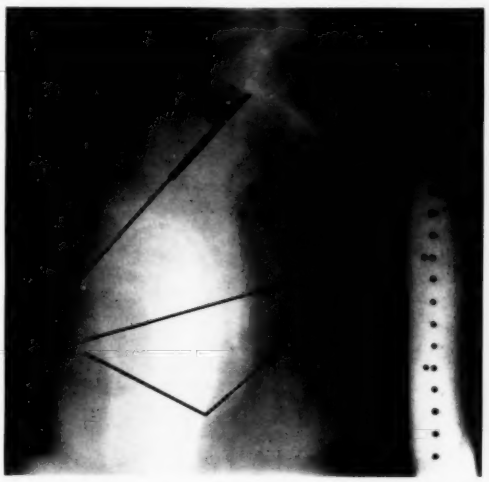


Fig. 2. Lateral roentgenogram diameters as shown in Figure 9. (Correction scale at side)

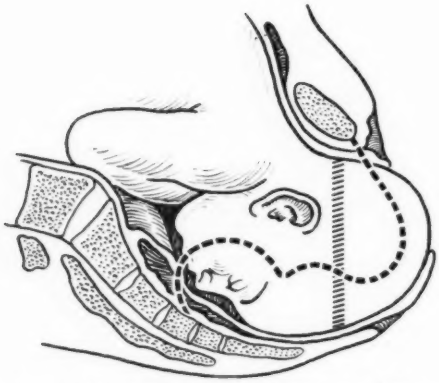


Fig. 3. With the head flexed at the perineum before extension and disengagement take place the occipital part of the head comes in contact with the pubic arch, meeting resistance at the parietal bosses (Fig. 4). (Modified from DeLee.)

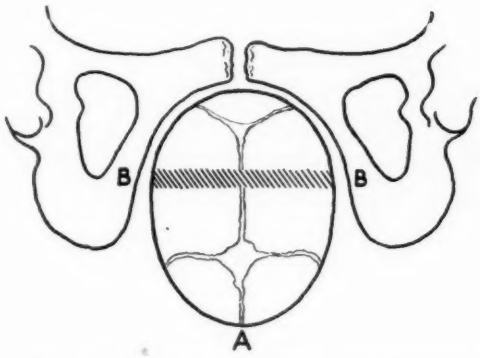
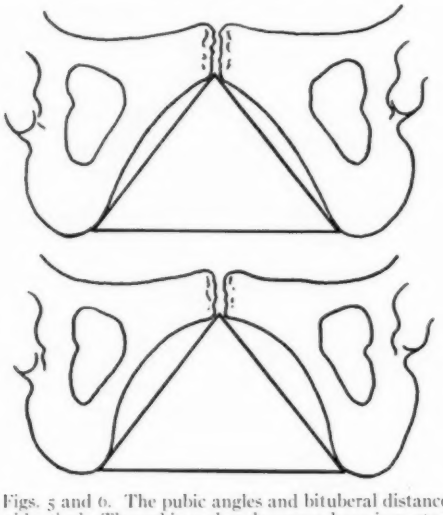


Fig. 4. When the fetal head begins to extend the parietal bosses meet resistance at *B-B*, and point *A* sweeps upward over the perineal floor. (Modified from DeLee.)

these head and outlet relationships that the width of the subpubic angle and the shape of the pubic arch are of considerable importance. As Allen logically states, "The important point is clearly how close the occiput is allowed to approach the lower edge of the symphysis."

If we consider variations in the downward course of the pubic rami, it becomes evident that the degree of the pubic angle in itself may



Figs. 5 and 6. The pubic angles and bituberal distances are identical. The pubic arches, however, have important differences from the obstetrical viewpoint.

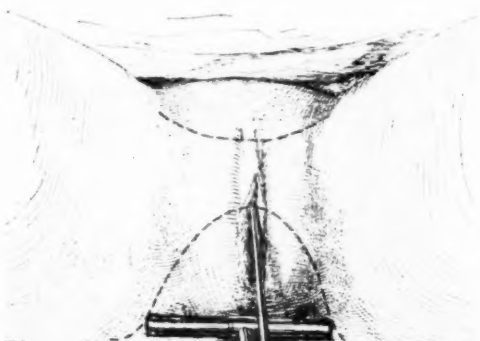


Fig. 7. The sliding crossbar of a Thoms outlet pelvimeter has been replaced by a solid bar 9 centimeters in length. After palpation of the arch this bar is brought to fit snugly between the rami. It is held in this position while the arm of the pelvimeter is placed at the lower edge of the symphysis. The symphysis biparietal distance is read from the scale. The sacral biparietal distance is measured by holding the cross-bar in position and swinging the arm posteriorly to the sacrococcygeal junction—1 centimeter is deducted from the reading to compensate for the thickness of the lower sacrum. (Modified from Williams.)

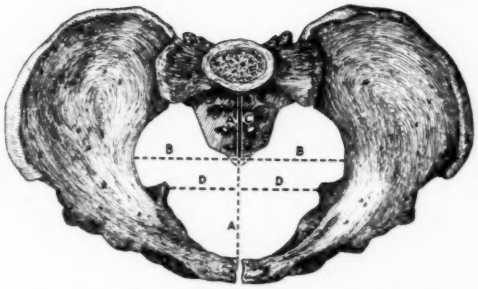


Fig. 8. The pelvic inlet: *A*, anteroposterior diameter, *B*, transverse diameter, *C*, posterior sagittal diameter, *D*, transverse diameter of midplane.

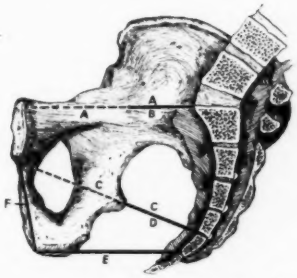


Fig. 9. Anteroposterior diameters seen in lateral aspect: *A*, anteroposterior diameter of inlet, *B*, posterior sagittal diameter of inlet, *C*, anteroposterior diameter of midplane, *D*, posterior sagittal diameter of midplane, *E*, sacral-biparietal distance, *F*, symphysis-biparietal distance.

not give a good index to outlet capacity and may even be misleading. Figures 5 and 6 illustrate this point. In both instances identical pubic angles are shown with the same intertuberal diameters, yet the available space in the upper part of the two arches is quite different.

As an alternative to determining the subpubic angle and attempting to determine a transverse outlet diameter, the measurement of the symphysis-biparietal distance has been recommended by Allen. This is the distance within which a normal biparietal diameter cannot approach the lower edge of the symphysis. This author determines this dimension from a roentgenographic film, but I am convinced that equally good information can be determined adequately by the palpatory method here described. Because of the difficulties previously commented upon of measuring the bituberous diameter, I find myself quite in agreement with this same author, who says "The bituberous diameter between the inner surfaces of the ischial tuberosities has also been discussed previously and the conclusion was then reached that this diameter could not satisfactorily be measured by any method so far described. The diameter, furthermore, is not of great importance *per se*, except in so far as it represents the free posterior end of the pubic arch: contraction of the arch always means a reduction in the intertuberous diameter, and since the arch can be more accurately measured, there seems to be little point in measuring the bituberous." From the roentgenological determination of the symphysis-biparietal distance. Allen recommends a special film using Chassard and Lapine's technique. He uses 10 centimeters as representing the normal biparietal distance, a figure slightly larger than the average of 93 millimeters given by Scammon and Calkins. In the pelvimeter here presented I have used a crossbar of 9 centimeters, allowing thereby about 0.5 centimeter for the thickness of the soft parts covering the pubic rami in their medial aspect.

METHOD

The patient is brought well down over the edge of the examining table in the lithotomy position; the arch is thoroughly palpated, by using both hands simultaneously as in the manner well described in textbooks. The course of the rami downward is noted, whether straight, moderate, or widely arcuate. The crossbar of the pelvimeter is then passed between the rami, and by upward pressure it is brought as near the symphysis as possible. As the crossbar is held in this position, the end of the arm of the pelvimeter is brought to the lower edge of the symphysis and the symphysis-biparietal distance read on the scale as shown (Fig. 7).

Another outlet dimension which should prove useful is the sacral-biparietal distance; that is, the distance from the lower terminus of the symphysis-biparietal distance, as described, to the tip of the sacrum. This can be measured externally with the pelvimeter or it can be determined satisfactorily on the lateral film used in the general pelvic survey. This is

accomplished by measuring downward between the shadows of the descending pubic rami the symphysis-biparietal distance previously determined. From the lower terminus of this distance to the tip of the sacrum represents the sacral-biparietal distance. The author is aware that the shadows of the pubic rami do not lie in the same plane and that the mean distance between them probably does not exactly represent the sagittal plane of the body. However, if films are taken at a target-film distance of 36 inches as recommended, the error encountered would not be obstetrically significant. For a further discussion of this aspect of roentgen pelvimetry the reader is referred to the author's views published elsewhere (3).

It might be useful to consider the relationship of these proposed outlet dimensions to a general pelvic survey. Such a survey for determining the adequacy of the bony pelvis for childbearing should include roentgen and palpatory methods (4). The former should include two flat films, one showing the birth canal from above downward, from which certain inlet and midplane measurements may be determined, and a second film taken laterally from which certain inlet, midplane, and outlet measurements may be obtained. The importance of morphological characteristics should also be emphasized in any such survey and, in addition, the following pelvic measurements will give useful information (Figs. 1, 2, 8, 9):

Pelvic inlet—Anteroposterior, transverse, posterior sagittal diameters

Pelvic midplane—Anteroposterior, transverse, posterior sagittal diameters

Pelvic outlet—Symphysis-biparietal, sacral-biparietal distances

In conclusion, the author takes this opportunity to mention again that the technical cost of such a pelvic survey need be hardly more than many hospital laboratory procedures, and that the information thus obtained is so greatly useful that every primigravid woman should have its benefit.

SUMMARY

1. Pelvic outlet pelvimetry at present is not satisfactory because transverse dimensions cannot be accurately determined.

2. The important information in a given case should reveal how close will be the approach to the lower edge of the symphysis of the biparietal diameter of the child's head as it passes through the pelvic arch.

3. This information may be secured by palpation, and with the pelvimeter here described.

4. The comprehensive pelvic survey should include inlet, midplane, and outlet dimensional information, by use of both palpatory and roentgen methods. Prognosis on the information so obtained should be solely the responsibility of the obstetrician.

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4. Thoms, H., and Wilson, H. M. Yale J. Biol., 1941. 13:831.

EDITORIAL

SURGERY
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SEPTEMBER, 1946

THE ABSORBABLE HEMOSTATIC AGENTS

THE absorbable hemostatic agents which have been recently developed, such as fibrin foam, oxidized cellulose (cellulosic acid), and gelatin sponge, represent a helpful contribution to the technique of surgery. Until these materials became available, muscle had been used as a hemostatic agent by the neurosurgeons since its introduction by Cushing in 1911. Most of the clinical experience with these new hemostatic agents, especially the fibrin foam and gelatin sponge, has been in neurosurgery. These reports have stimulated an interest in utilizing these materials to meet the varied problems of hemostasis in general surgery. Enough data are now available and more will soon be published which establish the usefulness of these agents in the broad field of surgery.

The fundamental mechanism involved in the use of the hemostatic agents is to hasten the formation of a clot and give structural support to the clot. This permits control of hemorrhage of a greater magnitude than could be expected from the normal protective mechanism—the physiological process of the clotting of blood. In using hemostatic agents one is merely enhancing the value of a protective mechanism of the body.

The particular field of usefulness of the hemostatic agents is in the control of hemorrhage where ligature or suture is not adequate or feasible. *There is no place for controversy over the matter of using these materials in lieu of ligature or suture* in the ordinary routine technique of surgery.

In dissecting away scar tissue, freeing adhesions, or in mobilizing large flaps one may have a continuously oozing surface which may be difficult to control except by these agents. In the first aid treatment of hemorrhage from surface wounds, especially from large veins, these materials should be very helpful as a temporary expedient until the patient can be cared for in an adequately equipped operating room. In hemorrhage from parenchymatous organs, such as in wounds or resections of the liver, there is a place for better hemostasis than can be obtained by ligature or suture alone. This is also true for the bleeding from the under surface of the liver after cholecystectomy.

One may encounter a sudden venous hemorrhage during the course of an operative procedure, such as in the mobilization of an organ or tumor, where the bleeding point cannot be identified for application of a hemostat because of the massive bleeding or the inadequacy of the exposure. In such trying situations the hemostatic agents offer an alterna-

tive to the blind application of hemostats which may damage adjacent vital structures or fail to prevent exsanguination. It has been customary in the past to resort to large gauze packs in an attempt to control such bleeding. When these packs are subsequently removed one may again encounter hemorrhage. In using the absorbable hemostatic materials one does not have to contend with this problem.

In operations on the bile ducts or in resections of the pancreas one may open the portal vein. If vein suture is not feasible the only alternative is ligation, which of course is most undesirable. In such circumstances, as well as in injury to other veins which one may not choose to ligate and where vein suture may not be feasible, the hemostatic agents may offer an alternative which may prove most helpful. In an experimental study one of these agents has been used to control hemorrhage from the vena cava of animals by the application of a "patch" such as is used by the neurosurgeons in dealing with hemorrhage from the dural sinuses. It is desirable in this "patch" technique on veins to cover the hemostatic agent with a layer of tissue such as the peritoneum or pleura to prevent dislodgment even though the "patch" may become quite firmly adherent to the vein within twenty to thirty minutes. If vein suture is feasible in an injury to a large vein there is also a place for the hemostatic agents as a secondary line of defense against leakage and hematoma formation.

Only a few of the situations where the absorbable hemostatic agents may be helpful have been outlined. The entire field of surgery abounds with problems which may be aided by these materials. For example, experimental studies are being conducted to ascertain their usefulness in the control of hemorrhage from the heart and the aorta where they may possibly have some value.

The several hemostatic agents have different physical properties and some variation in the rate of absorption. The fibrin foam and the gelatin sponge are similar in that they are a spongy material. The oxidized cellulose has the texture of ordinary gauze or cotton. In the dry state the fibrin foam is brittle and easily fragmented, whereas the gelatin sponge can be compressed by the fingers into a pliable sheet. The fibrin foam may be slightly stronger than the gelatin sponge when moistened. Under favorable conditions the fibrin foam or the gelatin sponge undergo absorption within about four to five weeks. The oxidized cellulose is absorbed more rapidly. In the presence of infection the gelatin sponge may become liquefied and disappear within a few days to a week. When oxidized cellulose comes in contact with blood it turns brown and then black. Fibrin foam or gelatin sponge take on a pink or red color when blood is taken up by the myriads of interstices.

There is as yet relatively little information to guide one in the selection of the agent best suited to a particular hemostasis problem in general surgery. As more clinical and experimental data become available it may be possible to work out a recommendation to cover the various situations in which one hemostatic agent may have more value than another.

There will undoubtedly be other absorbable hemostatic agents developed which may have properties that will be more useful for some of the hemostasis problems than the material now available. There is a place for a tougher and stronger spongy material as well as a place for a more rapidly absorbed spongy or foamy material, and possibly a more slowly absorbed material than is now at hand. This brings up the point that some official supervision should be given to the manufacture of the hemostatic agents so that standardization of absorption properties and sterility controls can be estab-

lished. It would be appropriate for a committee of the American College of Surgeons to make some recommendation on this.

Technical points which can best be described as "know how" but which cannot be easily put into words or diagrams, are essential for the successful use of these materials. One must gain some personal experience in handling these agents before attempting to use them for the control of a severe hemorrhage. The most important general feature of the technique of applying these materials is to permit fresh blood to soak into them and then apply firm even pressure over the bleeding area for from three to five minutes or longer, depending on the magnitude of the hemorrhage and the structure from which it comes. In some instances the hemorrhage may be controlled in less than a minute.

Thrombin solution has been used with these hemostatic substances to hasten the clot formation. Those who have used the fibrin foam and the gelatin sponge recommend soaking these agents in the thrombin solution before applying to the bleeding area. Some have used thrombin solution for soaking the oxidized gauze before use. According to one who has had the widest experience with oxidized cellulose the thrombin is not necessary or even desirable, as the best hemostatic effect is obtained by applying the material in the dry state. This is apparently due to the slightly acid reaction of the oxidized cellulose. Thrombin has been found to be ineffective in an acid medium. If one uses an alkaline solution for the sake of the activity of the thrombin, the particular hemostatic action of the cellulose which is a property of the acidity of the material is thereby negated. Some recent experimental work with gelatin sponge has demonstrated that it has excellent hemostatic properties *per se*. It may be used by soaking only in a physiological saline solution, and then expressing the excess saline. It may also be used in the dry state if it is first compressed in the fingers until it becomes pliable. If there is any defect in the normal clotting mechanism, such as a deficiency in prothrombin or platelets, it would be necessary to use a thrombin solution. In spite of this evidence on the hemostatic properties of the sponge without thrombin, it would probably be preferable to continue using the thrombin solution with gelatin sponge until further studies clarify the effectiveness of the thrombin in the hemostatic action of these materials.

When pressure is applied to these hemostatic agents after they have been saturated with fresh blood there is a tendency for the spongy material to adhere to the tissues to which it is applied, thus sealing off the hemorrhage. If the blood clots in the spongy material before the pressure is evenly applied or if a hematoma develops under the material it does not tend to adhere firmly and the bleeding may not be controlled. Under such circumstances it is better to try a fresh sponge and attempt to get more even pressure over the bleeding area.

The one most important limitation to these absorbable hemostatic agents is that one should not expect to put large amounts of these materials into wounds, especially if there is contamination or infection present, without having some undesirable sequelæ. When any new substance is used in surgery there are bound to be misuses which may reflect unfavorably on the material. The fundamental principle of minimizing the amount of foreign material in a wound applies to the hemostatic agents as well as to anything else. Therefore it is important to minimize the amount of hemostatic agent used and especially to employ as thin a layer of the agent as is compatible with obtaining satisfactory hemostasis. Where there is a massive hemorrhage

which might otherwise be fatal, the amount of material used is of course a minor consideration. When there is trivial bleeding which might cause an undesirable but not necessarily fatal hematoma, then one must weigh the problem of the disadvantages of a foreign material against the disadvantages of a hematoma.

The hemostatic agents are still in an experimental stage of development and clinical use. However, they are destined to have an important place in the armamentarium of the general surgeon as they have had for the neurosurgeon, and will necessarily constitute some part of the training program of the surgeon, the technical importance of which may be second only to the selection and use of ligatures and sutures.

The judicious use of the absorbable hemostatic agents will make for a greater degree of safety by minimizing blood loss in operative surgery, and furthermore may contribute to a widening of the scope of surgery, especially in the operative attack on malignant tumors in which the results being currently obtained by the accepted operative procedures on some organs leave much to be desired.

HILGER PERRY JENKINS.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE excellent monograph *Diseases of the Adrenals*[1] by Louis J. Soffer reviews completely the physiology and diseases of the adrenals. The chemical and mechanical techniques used in the diagnosis of adrenal disease, the recent methods used in studying the physiology of the glands, and the relation to other glands are discussed.

A detailed study is made of Addison's disease and of its treatment. The preoperative and postoperative treatment of surgical complications in Addison's disease are discussed. While pregnancy is strongly contraindicated in Addison's disease, the interruption of it is condemned as less safe than the attempt to carry it to termination. Advice is given for management.

The unusual sensitiveness of patients with Addison's disease to morphine, codeine, paraldehyde, bromides, barbiturates, insulin, thyroid extract, and thyroxin is emphasized. Epinephrine, sulfonamides, and penicillin may be used as in other patients.

An interesting paragraph is the summary of the experimental treatment of Addison's disease by transplantation of adrenal tissue. This should give successful results with improvements in transplantation technique, and would seem to be the ideal replacement therapy of the future.

The adrenogenital syndrome is also presented with critical discussion of virilism, Cushing's syndrome, adrenal cortical hyperplasia, and adrenal cortical tumors. The therapeutic measures include the use of various homones, irradiation therapy to the pituitary and adrenals, and surgery.

The medullary and other extracortical adrenal tumors, especially the pheochromocytoma are adequately discussed in this monograph, and the preoperative and postoperative treatment of the various types of tumors are clearly outlined.

It is a well written, concise, and practical book with an exceptionally complete bibliography. It can be recommended to clinicians and all those interested in the physiology of the adrenals.

ARTHUR J. ATKINSON.

IN four hundred odd pages, illustrated by seventy-two well chosen plates, Guthrie's *A History of Medicine*[2] covers the history of medicine in a distinctly interesting fashion. The volume is well documented with footnotes and a short list of authoritative publications follow each chapter. An appendix, containing a classified bibliography of medical history with a short evaluation of the more important ones, and a good index are included. Slightly more than half of the volume is devoted to the period ending with the 18th century. The 19th and 20th centuries are complete except that the author has chosen to leave for the evaluation of future historians the most recent advances in medicine and the work of those leaders who are still among the living.

While less exhaustive than Garrison's *Introduction to Medical History*, this volume has succeeded in combining broad philosophical discussion with brief biographical sketches in such a skillful manner as to encourage continuous reading. For the purpose of introducing the medical student to the study of medical history and for reviving the interest of the busy doctor in the fascinating story of medical progress, this volume is highly recommended. The experience of reviewing it has been a wholly enjoyable one.

THOMAS C. DOUGLASS.

THE second edition of *Clinical Electrocardiography*[3] by Scherf and Boyd is, as pointed out by the authors, primarily for the advanced student of electrocardiography and not for the beginner. It is well printed and there are only a few typographical errors. The electrocardiograms used as illustrations are numerous and for the most part satisfactory. Much of the text is used in discussing and explaining these cardiograms.

The authors adhere fairly well to the terminology recommended by the American Heart Association. They consider many clinical and controversial subjects and their approach to these subjects is stimulating. The discussion on interference dissociation and parasystole is well written. It would seem that more space could have been given to the subject of precordial leads and to coronary occlusion. The author's remarks regarding the changes incident to hypo-ovarianism will probably be challenged by some authorities.

This 250 page book is a definite contribution to the literature on this subject. It is to be recommended for the reference library of all physicians interested in electrocardiography.

JOHN A. MART.

[1] DISEASES OF THE ADRENALS. By Louis J. Soffer, M.D. Philadelphia, Lea & Febiger, 1946.

[2] A HISTORY OF MEDICINE. By Douglas Guthrie, M.D., F.R.C.S. (Ed.), F.R.S.E. With an Introduction by Samuel C. Harvey, M.D., F.A.C.S. Philadelphia, London, Montreal: J. B. Lippincott Co., 1946.

[3] CLINICAL ELECTROCARDIOGRAPHY. By David Scherf, M.D., F.A.C.P., and Linn J. Boyd, M.D., F.A.C.P. 2nd ed. New York: J. B. Lippincott Co., 1946.

CORRESPONDENCE

THE Rh FACTOR—SEROLOGIC BACKGROUND AND CLINICAL APPLICATION. —A Correction.

To the Editor: In the paper concerning the Rh Factor appearing in the June, 1946, issue of SURGERY, GYNECOLOGY AND OBSTETRICS, the sentence beginning on the eleventh line from the bottom of the page, in the right column of page 744, is misleading in that it states: "An individual whose blood is Rh-negative and who carries both Rh-positive and Rh-negative genes is heterozygot." The sentence should, of course, begin "An individual whose blood is *Rh-positive* . . .", as the presence of Rh-positive genes inevitably means that the individual's blood must be Rh-positive.

S. MILES BOUTON, JR.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgement must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

WILLIAM BEAUMONT'S FORMATIVE YEARS. Two Early Notebooks 1811-1821. By Genevieve Miller, M.A. New York: Henry Schuman, 1946.

COMPRESIONES MEDULARES NO TRAUMATICAS. By Rafael J. Babbini. Buenos Aires: Aniceto Lopez, 1943.

JOHN AND WILLIAM HUNTER. By Jane M. Oppenheimer, with a Foreword by Fenwick Beekman, M.D. New York: Henry Schuman, 1946.

CANCER OF THE SCROTUM IN RELATION TO OCCUPATION. By S. A. Henry, M.A., M.D. (Cantab.), F.R.C.P., D.P.H. (Cantab.). London, New York, Toronto: Oxford University Press, 1946.

PERIPHERAL VASCULAR DISEASES. By Edgar V. Allen, B.S., M.A., M.D., M.S., Nelson W. Barker, B.A., M.D., M.S., and Edgar A. Hines, Jr., M.D., B.S., M.A., M.S., with Associates in the Mayo Clinic and Mayo Foundation. Philadelphia, London: W. B. Saunders Co., 1946.

QUICK REFERENCE BOOK FOR MEDICINE AND SURGERY. By George E. Rehberger, A.B., M.D. 13th ed. Philadelphia, London, Montreal: J. B. Lippincott Co., 1946.

MOTHER AND BABY CARE IN PICTURES. By Louise Zabriskie, R.N. 3rd. ed. Philadelphia, London, Montreal: J. B. Lippincott Co., 1946.

DIABETIC CARE IN PICTURES. By Helen Rosenthal, B.S., Frances Stern, M.A. (Hon.), and Joseph Rosenthal, M.D. Philadelphia, London, Montreal: J. B. Lippincott Co., 1946.

LES NEPHROPATHIES GRAVIDIQUES. By H. Pigeaud and H. Dumont. Paris: Massonet C^ie, Editeurs, 1946.

LE FIBRO-MYOME UTERIN. By J. Ducuing. Paris: Masson et C^ie, Editeurs, 1946.

UROLOGIC ROENTGENOLOGY. By Miley B. Wesson, M.D. 2nd rev. ed. Philadelphia: Lea & Febiger 1946.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

W. EDWARD GALLIE, TORONTO, *President*
IRVIN ABELL, LOUISVILLE, *President-Elect*

Committee on Arrangements
THOMAS E. JONES, *Chairman;* JOHN W. HOLLOWAY, *Secretary*

CLINICAL CONGRESS TO BE HELD IN CLEVELAND DECEMBER 16 TO 20

THE thirty-second Clinical Congress of the American College of Surgeons, originally planned for New York from September 9 to 13 but postponed because of overlapping with the United Nations Assembly which will overtax hotel facilities, has now been scheduled for Cleveland, Ohio, from December 16 to 20. The change in place was necessary because suitable accommodations were not available in New York during the remainder of this year.

Cleveland has in its Public Auditorium superb facilities for the holding of most of the sessions and for the technical and educational exhibits. Certain official meetings, some of the panel discussions, and a few conferences, will be held in the Cleveland and Statler hotels where excellent accommodations are available. A clinical program in the Cleveland hospitals and Western Reserve University School of Medicine is also being developed by the Committee on Arrangements of which Dr. Thomas E. Jones is Chairman and Dr. John W. Holloway is Secretary.

This will be the first time that Cleveland has been host city to the Clinical Congress. A meeting was planned there in 1942 after the United States Army took over the Stevens Hotel in Chicago where the Congress had originally been scheduled. Later there was an announcement that the Cleveland Public Auditorium would also be needed by the War Department, and the 1942 Clinical Congress was voluntarily cancelled because of this and other war conditions.

Cleveland convention and hotel officials express great interest in the Clinical Congress as a contribution to the city's educational and scientific advancement. The Fellows are assured of a most congenial atmosphere in which to meet. The American College of Surgeons is well known and highly esteemed in Cleveland, as is natural in the home city of one of its most eminent founders, the late George Crile, Chairman of the Board of Regents for several years, and of many other honored Fellows, who have labored to develop the medical school and hospitals into maximum effectiveness in service to the sick and injured.

Cleveland has twenty-one hospitals approved by the American College of Surgeons. In several of these, operative and nonoperative clinics and demonstrations will be arranged during the week of the Congress. The preliminary clinical program will be published in a later issue.

As for the program that had been planned for New York for the scientific sessions, hospital conferences, and other events except clinics, this will be carried out in Cleveland with few, if any, changes. Up to the time of going to press there has not been opportunity to receive replies from all of the speakers who have been asked whether the change of time and place will affect their acceptance, but most responses have been in the affirmative, indicating that the program as outlined in succeeding pages will stand.

There is keen appreciation of the work done by the New York committe in preparing the clinical program there. While it cannot be used this year, it is hoped that it can be carried out at the 1947 Clinical Congress in New York.

FIRST POSTWAR CONGRESS

Following the same plan developed for the New York meeting, this first postwar Clinical Congress will differ from the meetings for several years prior to the war in that a return will be made to the original custom of holding the Presidential Meet-

ing on the opening evening, Monday, and the Convocation on the final evening, Friday, instead of combining them on the first night. This separation is especially desirable this year since exceptional interest will be centered on the Convocation as a result of the participation in the ceremonies of classes from 1942 through 1946.

PRESIDENTIAL MEETING

The Presidential Meeting will be held on Monday evening in the Music Hall of the Cleveland Public Auditorium. It will begin with the impressive processional of the officers, regents, and honorary guests. Dr. Thomas E. Jones, Chairman of the Committee on Arrangements, will give the address of welcome. Dr. W. Edward Gallie of Toronto, President of the College, will preside and will deliver the Presidential Address. An inaugural ceremony will be held for the incoming officers: Dr. Irvin Abell of Louisville, President; Dr. Leland S. McKittrick of Boston, First Vice-President; and Dr. F. Phinizy Calhoun, Atlanta, Second Vice-President. Foreign guests will then be introduced.

The first Martin Memorial Lecture will be a new feature to be included in the Presidential Meeting this year. The invitation to give this lecture has been accepted by Dr. Edward D. Churchill of Boston. This lectureship was established upon motion of the Board of Regents at its midyear meeting on April 1, as a memorial to both Dr. Franklin H. Martin and Mrs. Martin. The founder of the College and of SURGERY, GYNECOLOGY AND OBSTETRICS was joined by his wife in making the College the beneficiary at their deaths of the Journal, together with its physical plant operated by the Surgical Publishing Company of Chicago, of which they were the owners. Doctor Martin died in 1935 and Mrs. Martin in 1945.

The Martin Memorial Lecture, to be given annually during the Clinical Congress, and dealing with a scientific subject of the author's choosing, will supplant the Annual Oration in Surgery.

CONVOCATION

The Convocation scheduled for Friday evening, will open with a processional of officers, regents, and governors. The President, Dr. Irvin Abell, will preside and will make the opening remarks, confer the honorary fellowships, and present the candidates for fellowship.

An Assembly of Initiates will be held prior to the Convocation on Friday in order to instruct them in the Convocatian procedure and other matters. On this occasion the initiates will sign the fellowship roll.

Several hundred surgeons who have been received into fellowship *in absentia* during the years in which no Convocation was held, will be added to the number of initiates for the current year who will be present to participate in the initiation ceremonies.

SCIENTIFIC SESSIONS

General Surgery

Eminent surgeons and specialists, recognized as authorities in their fields, will address the scientific sessions, to be held on Tuesday, Wednesday, and Thursday evenings. These will be conducted as symposia, and the subjects for the three nights will be as follows: Tuesday, "Care of the Patient Before and After Operation"; Wednesday, "Venous Thrombosis and Prevention of Pulmonary Embolism"; and Thursday, "Antibiotic and Chemotherapeutic Agents in Surgery." The annual Fracture Oration will be included in the Wednesday evening program.

Two major panel discussions will be held every afternoon except Thursday when the first panel will be omitted because of the annual meeting of the Fellows.

A symposium on fractures and other traumas will be held on Tuesday afternoon, and a symposium on cancer on Wednesday, from 2:00 to 4:00 o'clock.

Concurrent panel discussions are also planned on Friday afternoon for each of the following specialties: plastic surgery, thoracic surgery, urology, neurological surgery, orthopedics, and obstetrics. Outlines of the programs are published in succeeding pages.

Ophthalmology and Otorhinolaryngology

Ophthalmology panel discussions will be held Tuesday, Wednesday, and Thursday mornings at 11:00 o'clock on, respectively, "Retinal Detachment," "Glaucoma," and "Keraoplasty." On Tuesday evening at 8:00 o'clock there will be a symposium on "Orbital Reconstruction Including Prosthesis." On Thursday evening a scientific session is planned with the following as the subjects: "Recent Advances in Ophthalmology"; "Medical Treatment of Glaucoma"; and "Visual Disturbances Associated with Head Injuries."

Otorhinolaryngology panel discussions will be held Tuesday, Wednesday, and Thursday mornings at 11:00 o'clock on, respectively, "Treatment of Ménière's Disease," "Osteomyelitis of the Skull," and "Rehabilitation of War Deafness." On Tuesday evening at 8:00 o'clock there will be a symposium on "Treatment of Deafness" and on Thursday evening a symposium on "Surgery of the Nasal Accessory Sinuses."

Of interest to ophthalmologists, otorhinolaryngologists, and other surgeons will be a symposium to be held on Wednesday evening at 8:00 o'clock on "Plastic Surgery of the Head and Neck."

FORUMS ON FUNDAMENTAL SURGICAL PROBLEMS

The Forums on Fundamental Surgical Problems will be conducted on Tuesday, Wednesday, Thursday, and Friday mornings. Included in them will be brief reports of original clinical and experimental observations relating to the broad aspects of surgery and the surgical specialties. No prepared discussions of the reports are planned, but questions and comments will be invited. Especially keen interest is expected in these sessions this year because of the accumulation of the results of 5 years of work since the last Clinical Congress. Dr. Owen H. Wangensteen of Minneapolis, chairman of the committee which is planning the program, is working toward representation of as many as possible of the various university departments of surgery in this presentation of clinical and experimental research work.

The enlistment of the interest of young men who are doing original work, through the forums, is one of the most beneficial results of these sessions which are now considered to be an indispensable feature of every Clinical Congress.

HOSPITAL CONFERENCE

Dr. W. Edward Gallie, President of the College, will address the opening session of the twenty-fifth annual Hospital Standardization Conference on Monday morning at 10:00 o'clock in the Auditorium; and will preside at the meeting, which will be attended by surgeons and hospital representatives. Following Dr. Gallie's résumé of the Hospital Standardization program of the College, including plans for the future, there will be reports on the progress of the 1946 Hospital Standardization survey, final results of which, including the Approved Lists of hospitals, cancer clinics, and approved hospitals for graduate training in surgery, will be announced at the end of the year, instead of at the Clinical Congress as was the practice in former years.

The remainder of the Monday morning session will be devoted to talks by medical and hospital authorities on advances in medicine and surgery as they affect the postwar hospital, with particular consideration of their relation to the Hospital Standardization program.

The afternoon conference on Monday will be concentrated upon current problems and the outlook for the future in nursing service. The Tuesday morning conference will have as its main subject personnel management, and the Tuesday afternoon session will be centered around personnel problems in specific fields, such as dietary, laboratory, medical records, medical social service, x-ray, physical and occupational therapy, and other professional and semi-professional services. The discussions will emphasize the importance of scientific management techniques in assuring high quality service from personnel.

The Wednesday morning conference will have as its main theme the importance of assuring high standards of care to the community and patients through providing in the general hospital facilities for all types of illness. The subject will be discussed from the standpoint of psychiatric, tuberculous, cancer, chronically ill, and convalescent patients. The Wednesday afternoon conference will center mainly around discussion of ways of improving co-operation between general hospitals and special hospitals in the care of all types of special patients.

The Thursday morning conference will revolve around the physical plant of the hospital and the importance of improvement and modernization in raising standards of care of the patient. New mechanical and technical developments will be presented. The afternoon conference will discuss the hospital as the health center of the community, with consideration of the effects of this concept upon hospital public relations and upon the progress of preventive medicine and public health.

An evening conference will be held at 7:30 o'clock on Tuesday. This will be devoted to discussion of the responsibilities of trustees, and members of governing boards will be especially invited to attend and to participate. A conference will be held on Wednesday evening also. This will be a round table conference on responsibilities of hospital administrators, and the preparation which is necessary to enable them to cope successfully with the wide range of administrative problems. The discussion of these problems will interest all hospital personnel.

ANNUAL MEETING OF FELLOWS

The annual meeting of the Governors and Fellows will be held on Thursday afternoon at 1:45. There will be election of officers and governors. The annual meeting affords the Fellows of the College an opportunity to hear reports of officials on the work of the organization, and to learn how it has not only raised the professional and ethical standards of surgery, but has also promoted good hospitalization and general improvement in the practice of medicine in the United States and Canada. Each Fellow has a

personal part in this work and may extend the influence of the College materially in his local community. Hospital Standardization alone offers him unlimited opportunity to provide better medical care for his patients in the hospital in which he works through continuous progress in applying the principles of the Minimum Standard which insure the best care of the patient.

Every Fellow will want to attend this important meeting, at which reports will be presented on financial affairs; Hospital Standardization; Graduate Training in Surgery; Medical Motion Pictures; Publications; Public Relations; Library and Literary Research; the work of the state and provincial credentials committees, committees on applicants, and the Committee on History Reviews; Sectional Meetings, 1946; and the Department of Clinical Research, including cancer clinics, Medical Service in Industry, the Committee on Cancer, and the Committee on Fractures and other Traumas. Dr. Abell will report on administration of the College, staff changes, and retirements, and Dr. Arthur W. Allen, Vice-Chairman of the Board of Regents will discuss "Fellowships, Obligations and Opportunities."

STATE AND PROVINCIAL EXECUTIVE, CREDENTIALS AND JUDICIARY COMMITTEES

On Wednesday morning from 9:00 to 12:00 o'clock the State and Provincial Executive, Credentials, and Judiciary committees will meet to discuss their respective activities.

MEDICAL MOTION PICTURES

The latest available films showing surgical procedures and related subjects will be shown in the medical motion picture exhibits which will be held daily. These are a much appreciated feature of the Clinical Congress. Despite the decrease in production of such films during the war period, a surprising number of new pictures on varied subjects are being received by the American College of Surgeons for review.

The schedule will be so arranged as not to conflict with either the clinical program at the hospitals or the scientific sessions. Both sound and silent, standard and color films will be shown, all of which have been approved by the Committee on Medical Motion Pictures.

TECHNICAL AND SCIENTIFIC EXHIBITION

The technical exhibit, together with the registration and clinic ticket bureaus, will be held in the Cleveland Public Auditorium. Leading manufacturers of surgical instruments, x-ray apparatus, sterilizers, operating room lights, ligatures, dressings, hospital apparatus and supplies of all kinds, pharmaceuticals, and publishers of medical books will be represented in the exhibition. The technical exhibits will demonstrate many of the newer features learned from our experience in the war.

ADVANCE REGISTRATION

The hospitals of Cleveland afford accommodations for a considerable number of visiting surgeons. However, in order to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the meetings and also by accommodations in the hotels. It is therefore expected that surgeons who wish to attend the Congress will register in advance.

Fellows of the College whose dues are paid to December 31, 1945, initiates of the classes of 1942, through 1946, and Fellows in military service will not be required to pay a registration fee for the Clinical Congress in Cleveland. Checks that have already been sent for the New York Congress are being returned. For endorsed junior candidates the fee is $5.00. Surgeons, not Fellows, who attend as invited guests of the College, will pay a registration fee of $10.00.

CLEVELAND HOTELS AND THEIR RATES

Although the hotel situation in Cleveland seems more favorable than in many other cities, it is nevertheless essential to make reservations as far in advance as possible. Following is a list of the principal hotels:

	No. of Rooms	Rates
The Alcazar, Surrey and Derbyshire Roads	200	$3.00 up
Hotel Allerton, E. 13th St. & Chester Ave.	600	2.65 up
Hotel Auditorium, E. 6th & St. Clair Ave.	300	2.00 up
Belmont Hotel, Euclid Ave. at E. 40th St.	200	2.00 up
Hotel Bolton Square, Carnegie at E. 89th St.	300	2.50 up
Carter Hotel, 1012 Prospect Ave.	600	4.00 up
Hotel Cleveland, Public Sq. & Superior Ave.	1,000	3.00 up
Fenway Hall Hotel, Euclid Ave. at Univ. Circle	400	3.00 up
The Hollenden, Superior Ave. at E. 6th St.	1,000	3.00 up
Lake Shore Hotel, 12506 Edgewater Dr.	450	3.50 up
New Amsterdam Hotel, Euclid Ave. at E. 22nd St.	300	2.00 up
Hotel Olmsted, E. 9th St. & Superior Ave.	250	3.00 up
Park Lane Villa, E. 105th & Park Lane Ave.	400	3.00 up
Sovereign Hotel, 1575 E. Blvd.	300	2.50 up
Hotel Statler, Euclid Ave. at E. 12th St.	1,000	3.00 up
Tudor Arms Hotel, Carnegie at E. 107th St.	200	3.50 up
Wade Park Manor, E. 107th & Park Lane	400	3.50 up
The Westlake, Blount St., Rocky River	400	3.00 up

CLINICAL CONGRESS PROGRAM IN BRIEF

Monday

10:00 General Assembly for Surgeons and Hospital Representatives
1:30–3:00 Panel Discussion
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Hospital Conference
1:00 Surgical Film Exhibition (General)
3:30–5:00 Panel Discussion
8:00 Presidential Meeting

Tuesday

9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
10:00 Hospital Conference
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat)
9:30–12:00 Forum on Fundamental Surgical Problems,
10:00 Surgical Film Exhibition (General)
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
1:30–3:00 Panel Discussion
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Hospital Conference
2:00 Symposium on Fractures and Other Traumas
2:00 Surgical Film Exhibition (General)
3:30–5:00 Panel Discussion
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat)
7:30 Hospital Conference—Trustees
8:00 Scientific Session, General Surgery
8:00 Scientific Session, Ophthalmology
8:00 Scientific Session, Otorhinolaryngology

Wednesday

8:00 Meeting of Cancer Committee
9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected Local Hospitals
9:30 Hospital Conference
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat)
9:30–12:00 Forum on Fundamental Surgical Problems,
10:00 Surgical Film Exhibition (General)
State and Provincial Committees:
9:30 Judiciary Committees
10:00 Executive Committees
10:30 Credentials Committees and Committees on Applicants
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
12:00 Meeting of Board of Governors
1:30–3:00 Panel Discussion
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Symposium on Cancer
2:00 Surgical Film Exhibition (General)
2:30 Hospital Conference
3:30–5:00 Panel Discussion
6:00 Vandyck Reunion Dinner
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat)
7:30 Hospital Conference
8:00 Scientific Session, General Surgery
8:00 Scientific Session (Eye, Ear, Nose and Throat)

Thursday

9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
9:30 Hospital Conference
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat)
9:30–12:00 Forum on Fundamental Surgical Problems
10:00 Surgical Film Exhibition (General)
11:00 Panel Discussions
Ophthalmology
Otorhinolaryngology
1:30 Adjourned Meeting, Governors
1:45 Annual Meeting, Fellows
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00 Hospital Conference
3:00 Panel Discussion—Graduate Training in Surgery,
3:30–5:00 Panel Discussion
3:30 Surgical Film Exhibition (General)
3:30 National and Regional Fracture Committees,
4:00 Committee on the Library
7:00 Surgical Film Exhibition (Eye, Ear, Nose and Throat)
8:00 Scientific Session, General Surgery
8:00 Scientific Session, Ophthalmology
8:00 Scientific Session, Otorhinolaryngology,

Friday

9:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
9:30 Surgical Film Exhibition (Eye, Ear, Nose and Throat)
9:30–12:00 Forum on Fundamental Surgical Problems
10:00 Surgical Film Exhibition (General)
1:30–3:00 Panel Discussion, Surgery of the Stomach
2:00 Clinics, Demonstrations and Clinical Group Conferences, Selected local hospitals
2:00–4:00 Panel Discussions
Obstetrics
Plastic Surgery
Neurological Surgery
Thoracic Surgery
Urology
Orthopedic Surgery
2:00 Surgical Film Exhibition (General)
3:30–5:00 Panel Discussion, Surgery of the Vascular System.
8:00 Convocation

EVENING SCIENTIFIC SESSIONS

GENERAL SURGERY

Tuesday

Care of the Patient before and after Operation

Fluid and Electrolyte Balance. CARL MOYER, Eloise, Michigan.
Nutritional Preparation of the Substandard Risk Patient. RICHARD L. VARCO, Minneapolis.
Use of Blood and Blood Substitutes. JOHN D. STEWART, Buffalo.
Blood Transfusion Problems, with Special Reference to the Rh Factor. ALEXANDER S. WIENER, Brooklyn.
Safe Conduct of the Patient Through Operation. OWEN H. WANGENSTEEN, Minneapolis.

Wednesday

Venous Thrombosis and Prevention of Pulmonary Embolism

Interruption of Deep Veins. ARTHUR W. ALLEN, Boston.
Sympathetic Nerve Block. ALTON OCHSNER, New Orleans.
Anticoagulants. D. W. GORDON MURRAY, Toronto.

Fracture Oration

Modern Methods in the Treatment of Fractures. EDWIN W. RYERSON, Chicago.

Thursday

Antibiotic and Chemotherapeutic Agents in Surgery

Pathologic Physiology of Surgical Infections. JOHN S. LOCKWOOD, New Haven.
Penicillin—Its Use in Surgery and Influence on Earlier Types of Chemotherapy. WILLIAM A. ALTEMEIER, Cincinnati.
Streptomycin. HORTON C. HINSHAW, Rochester.
Correlation of the Use of Antibiotic and Chemotherapeutic Agents with General Principles of Surgery. CHAMP LYONS, New Orleans.

OPHTHALMOLOGY

Tuesday

Orbital Reconstruction Including Prosthesis

Acrylic Prosthesis. A. D. RUEDEMANN, Cleveland.
Basket Implant. NORMAN L. CUTLER, Wilmington.
Orbital Measurements.
Reconstruction of Upper Lid and Orbital Floor Defects. Major ARTHUR E. SHERMAN, Springfield Missouri.

Thursday

Surgical Applied Anatomy in Eye Surgery. MEYER WIENER, Coronado.
Visual Disturbances Associated with Head Injuries. JOHN MCGAVIC, Fort Madison.

OTORHINOLARYNGOLOGY

Tuesday

Treatment of Deafness

The Suppurating Ear.
The Fenestration Operation. GEORGE E. SHAMBAUGH, JR., Chicago
Use of Radium for Conductive Deafness. JOHN E. BORDLEY, Baltimore.

Thursday

Surgery of the Nasal Accessory Sinuses

Indications for Surgery in the Light of the Use of Antibiotics.
Intranasal Surgery. JOHN J. SHEA, Memphis.
External Operations.

SYMPOSIUM ON PLASTIC SURGERY OF THE HEAD AND NECK

Wednesday 8 p.m.

Cancellous Bone Grafts to the Jaw.
Repair of Nasal Defects with Free Composite Grafts of Skin and Cartilage from the Ear. JAMES B. BROWN, St. Louis.
Studies in the Anatomy and the Repair of Cleft Palate.
Preservation of Function Following Resections of Jaw Tumors.

PANEL DISCUSSIONS

GENERAL SURGERY

Monday, 1:30–3:00 p.m.

Rehabilitation of the Surgical Patient and Early Ambulation. Leader, HOWARD RUSK, New York.

Monday, 3:30–5:00 p.m.

The Treatment of Cancer of the Large Bowel. Leader, FREDERICK A. COLLER, Ann Arbor.

Tuesday, 1:30–3:00 p.m.

Thiouracil in Thyroid Disease. Leader, FRANK LAHEY, Boston.

Tuesday, 3:30–5:00 p.m.

Recent Trends in the Management of Carcinoma of the Cervix. Leader, JOE VINCENT MEIGS, Boston.

Wednesday, 1:30–3:00 p.m.

Anesthesia. Leader, HENRY K. BEECHER, Boston.

Wednesday, 3:30–5:00 p.m.

Protein Metabolism in the Surgical Patient. Leader, ROBERT ELMAN, St. Louis.

Thursday, 3:30–5:00 p.m.

Spinal Cord Injuries. Leader, HOWARD C. NAFFZIGER, San Francisco.

Friday, 1:30–3:00 p.m.

Surgery of the Stomach. Leader, ROSCOE R. GRAHAM, Toronto.

Friday, 3:30–5:00 p.m.

Surgery of the Vascular System. Leader, DANIEL C. ELKIN, Atlanta, Georgia.

SURGICAL SPECIALTIES

Friday 2:00—5:00

Orthopedic Surgery Panel. (Subject to be announced.) Leader, CARL E. BADGLEY, Ann Arbor.
Urology Panel. (Subject to be announced.) Leader, HERMAN L. KRETSCHMER, Chicago.
Plastic Surgery Panel. (Subject to be announced.) Leader, ROBERT H. IVY, Philadelphia.
Neurological Surgery Panel. (Subject to be announced.) Leader, FRANCIS C. GRANT, Philadelphia.
Obstetrics Panel. (Subject to be announced.) Leader, FREDERICK C. IRVING, Boston.
Thoracic Surgery Panel. (Subject to be announced.) Leader, RICHARD H. SWEET, Boston.

OPHTHALMOLOGY

Panel discussions in the field of Ophthalmology are planned for Tuesday, Wednesday, and Thursday mornings at 11:00 o'clock, on the following subjects: Retinal Detachment; Glaucoma; Keratoplasty.

OTORHINOLARYNGOLOGY

Panel discussions on subjects in the field of Otorhinolaryngology are planned for Tuesday, Wednesday and Thursday mornings at 11:00 o'clock on the following subjects, respectively: The Treatment of Ménière's Disease; Osteomyelitis of the Skull; Rehabilitation of War Deafness.

SYMPOSIUM ON FRACTURES AND OTHER TRAUMAS

AT 2:00 o'clock on Tuesday afternoon there will be held a symposium on Fractures and Other Traumas under the direction of Robert H. Kennedy of New York. This symposium will be devoted to a number of brief presentations by specialists n various fields concerning new or improved methods adopted during the war which are applicable to injury in civilian surgery. The aim is to give a rapid survey of worthwhile gains made during the war which may prove of lasting value in the field of trauma.

Among the fifteen or twenty short papers which are planned are the following:

Bone Grafts. GEORGE K. CARPENTER, Nashville.
Spinal Cord Injuries. DAVID H. POER, Atlanta.
Injuries to the Rectum. EDMUND J. CROCE, Worcester.
Transportation of Fractures. WILLIAM J. STEWART, Columbia.
Replacement of Skin Defects. JAMES B. BROWN, St. Louis.
Fractures of the Carpal Scaphoid. MATHER CLEVELAND, New York.
Amputations. RUFUS H. ALDREDGE, New Orleans.
Training of Amputees. HENRY H. KESSLER, Newark.
Rehabilitation. Col. A. WILLIAM REGGIO, Washington.
Compound Fractures Treated with Penicillin and Delayed Primary Closure. OSCAR P. HAMPTON, Jr., St. Louis.

SYMPOSIUM ON CANCER

A symposium on cancer is planned for Wednesday afternoon. The Cancer Committee of the College has done outstanding work in furthering the development of cancer clinics in hospitals and providing for the registration of cured cases of malignant disease in the cancer archives. The chairman of this committee will give a brief review of these activities of the College in opening the symposium.

Other subjects of practical interest are under consideration for inclusion in the program, which is being planned to interest surgeons, pathologists, and radiologists.